PLEASE BRING THIS PROGRAM WITH YOU

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Educational Objective

APSA's annual meeting is designed to provide four days of comprehensive continuing education in the field of pediatric surgery. APSA brings together the world's leading authorities to present and discuss the most recent clinical and research efforts.

The program will begin with two half-day symposia: the first dealing with bariatric surgery and the second addressing endoscopic surgery. Meeting attendees will also view and discuss videos and poster presentations on this day. The topics at these sessions have been selected jointly by the Program and Education committees and are based on member requests about what is relevant to their practices. The scientific sessions consist of basic research and practical clinical presentations. The poster sessions allow investigators an opportunity to share preliminary research.

This meeting covers the breadth of pediatric surgery and is intended to acquaint attendees with the latest research findings, clinical discoveries and trends that influence the dayto-day practice of pediatric surgery.

Accreditation

APSA is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

Credit Designation

APSA designates this educational activity for a maximum of 19.75 category 1 credits toward the American Medical Association Physician's Recognition Award. Each physician should claim only those credits he/she actually spent in the activity.

Policy on Faculty and Provider Disclosure

It is the policy of the ACCME and APSA that the faculty, program committee and sponsors disclose real or apparent conflicts of interest relating to the topics of the educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentations. If no conflicts are indicated, none have been disclosed.

Commercial Support

APSA would like to thank the *Journal of Pediatric Surgery* for its educational grant for the *Journal of Pediatric Surgery* Lecture and its educational grant for the transcription of the annual meeting technical sessions. APSA also thanks the current sponsors and exhibitors for their unrestricted educational grants.

Meeting Sponsors

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2005 Exhibitors

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Exhibit Hours

Monday, May 30 Tuesday, May 31 6:30 a.m. – 1 p.m. 7 a.m. – 2 p.m.

APSA Planning Committees

APSA would like to thank the following people for their contribution to the APSA annual meeting program:

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* Dr. Crombleholme has received grants/research support from NICHD and NIAMS.

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*Dr. Harmon is a consultant for Stryker Endoscopy.

Committee Meetings

The following is a listing of committee meetings during the APSA Annual Meeting:

Friday, May 27			
Noon – 9 p.m.	Pediatric Surgery Training Directors	Grand Canyon 9/10	
Saturday, May 2	28		
9 a.m. – 5 p.m.	APSA Board of Governors	Desert Conference Suite II	
3:30 – 5 p.m.	Practice Committee	Grand Sonoran H	
4 – 6 p.m.	AAP Program Committee	Grand Sonoran I	
6 – 10 p.m.	Publications Committee	Desert Conference Suite IV	
Sunday, May 29)		
6:30 – 8 a.m.	Trauma Committee	Grand Sonoran J	
6:30 – 8 a.m.	Ethics and Advocacy Committee	Grand Sonoran H	
6:30 – 8 a.m.	Outcomes & Clinical Trials Committee	Grand Sonoran K	
6:30 – 8 a.m.	Education Committee	Desert Conference Suite VI	
7 – 8 a.m.	Cancer Committee	Grand Sonoran I	
7 – 8 a.m.	Pectus Multicenter	Desert Conference Suite IV	
Monday, May 30			
6:30 – 7:30 a.m.	Informatics and Telemedicine Committee	Grand Sonoran I	
6:30 – 7:30 a.m.	Task Force on Family Issues	Grand Sonoran J	
6:30 – 7:30 a.m.	Workforce Committee	Grand Sonoran K	
6:30 – 7:30 a.m.	APSA Foundation Board of Directors	Grand Sonoran H	
6:30 – 7:30 a.m.	Ethics Teaching Project	Desert Conference Suite IV	
6:30 – 7:30 a.m.	Membership and Credentials Committee	Desert Conference Suite VI	
1 – 2 p.m.	Florida Association of Pediatric Surgeons	Grand Sonoran J	
4 – 5:30 p.m.	ACS Advisory Council for Pediatric Surger	y Grand Sonoran I	
5 – 6:30 p.m.	<i>Journal of Pediatric Surgery</i> Editorial Board Reception	Grand Sonoran J & K	
Wednesday, June 1			

Noon – 3 p.m.	Executive Council for Pediatric Surgery	Grand Sonoran H
	Organizations	

Schedule at a Glance

Friday, May 27		Room
Noon – 9 p.m.	Pediatric Surgery Training Directors meeting	Grand Canyon 9/10
Saturday, May 28		
9 a.m. – 5 p.m.	APSA Board of Governors meeting	Desert Conference Suite II
1 – 5 p.m.	Committee meetings	Grand Sonoran H, I, J, K
3 – 6 p.m.	Registration open	East Registration Desk
6 – 10 p.m.	Publications Committee meeting/dinner	Desert Conference Suite IV
6:30 – 10 p.m.	APSA Board of Governors dinner	Roy's Restaurant
Sunday, May 29		
6:30 – 8 a.m.	Committee meetings	Grand Sonoran H, I, J, K Desert Conference Suites IV & VI
7 a.m. – 5:30 p.m.	Registration open	East Registration Desk
8 – 10:30 a.m.	Symposium: Bariatric Surgery	Grand Sonoran E/F
10:30 – 11 a.m.	Refreshment break	Grand Sonoran Foyer
11 a.m. – Noon	International Surgical Education Pa	nel Grand Sonoran E/F
12:30 – 1:30 p.m.	Lunch with video session	Grand Sonoran E/F
12:30 – 2:30 p.m.	Poster set-up	Grand Sonoran A/B Grand Sonoran C/D
2 – 4:30 p.m.	Symposium: Endoscopic Surgery	Grand Sonoran E/F
3:30 – 6 p.m.	Posters open for viewing	Grand Sonoran A/B Grand Sonoran C/D
4:30 – 6 p.m.	Poster Presentations/ Poster Viewing Area: (authors in attendance)	Grand Sonoran A/B Grand Sonoran C/D
5:30 – 6:30 p.m.	Exhibit set-up	Grand Sonoran Foyer
6:30 – 8:30 p.m.	Welcome Reception	Ballroom Lawn
Monday, May 30		
6 – 7:30 a.m.	Annual 5K Fun Run	Ballroom Entrance
6:30 – 7:30 a.m.	Committee meetings	Grand Sonoran H, I, J, K Conference Desert Suites IV & VI
6:30 a.m. – 1 p.m.	Registration open	East Registration Desk
6:30 a.m. – 1 p.m.	Posters and Exhibits open for view	ing Grand Sonoran A/B; C/D Grand Sonoran Foyer

6:30 – 7:30 a.m.

7:30 – 9:15 a.m.

Grand Sonoran Foyer

Grand Sonoran E/F

Continental breakfast in the exhibits area

Welcome/Scientific Session I

Schedule at a Glance (Continued)

Monday, May 30	(Continued)	Room
9:15 – 10:15 a.m.	Robert E. Gross Lecture <i>W. Hardy Hendren, M.D.</i> "Looking Back 50 Years"	Grand Sonoran E/F
10:15 – 10:45 a.m.	Refreshment break	Grand Sonoran Foyer
10:45 a.m. – Noon	Scientific Session II	Grand Sonoran E/F
Noon – 1 p.m.	International Guest Lecture <i>Prof. Frans Hazebroek, M.D., Ph.D.</i> "Is Continuation of Life Support Always Best Option for the Surgical Neonate?"	Grand Sonoran E/F
1:30 – 3 p.m.	Benji Brooks Meeting and Luncheon	Desert Conference Suite I
2 p.m.	Golf Tournament	Wildfire Golf Club
2 p.m.	Tennis Tournament	Tennis Center
3:15 – 8:30 p.m.	Cattle Drive Activity	Ballroom Entrance
6 – 11 p.m.	Optional Dining Shuttle	Ballroom Entrance
6:30 – 8 p.m.	New Member Reception (invitation only)	Presidential Suite

Tuesday, May 31

6:30 – 8 a.m.	Member Business Meeting and Breakfast	Grand Sonoran G
6:30 a.m. – 1 p.m.	Registration open	East Registration Desk
7 a.m. – 2 p.m.	Posters and Exhibits open for viewing	Grand Sonoran A/B, C/D Grand Sonoran Foyer
7 – 8 a.m.	Continental breakfast (nonmembers)	Grand Sonoran Foyer
8 a.m. – Noon	Sonoran Desert Hummer Tour	Ballroom Entrance
8 – 10 a.m.	Scientific Session III	Grand Sonoran E/F
10 – 10:30 a.m.	Refreshment break	Grand Sonoran Foyer
10:30 a.m. – Noon	Scientific Session IV	Grand Sonoran E/F
Noon – 1:15 p.m.	Welcome New Members/ Presidential Address <i>Robert J. Touloukian, M.D.</i> "The Ultimate Commencement"	Grand Sonoran E/F
1:15 – 1:30 p.m.	Refreshment break	Grand Sonoran Foyer
1:30 – 3:30 p.m.	Telesurgery demonstration with lunch	Grand Sonoran E/F
2 p.m.	Exhibits dismantle	Grand Sonoran Foyer
3:45 – 5:15 p.m.	COG Surgeons' Meeting (open to all APSA meeting attendees)	Grand Sonoran E/F
6:30 – 7:15 p.m.	President's Reception	Grand Sonoran Foyer
7:15 – 10:30 p.m.	President's Banquet	Grand Sonoran E/F

Schedule at a Glance (Continued)

Wednesday, June 1		Room
7 – 11:15 a.m.	Posters open for viewing	Grand Sonoran A/B Grand Sonoran C/D
7 – 8 a.m.	Continental breakfast	Grand Sonoran Foyer
7:30 – 11:30 a.m.	Registration open	East Registration Desk
8 – 8:15 a.m. 8:15 – 8:30 a.m.	APSA Foundation Scholars <i>Karl Sylvester, M.D.</i> "Liver Regeneration and Stem Cell Regulation via the WNT Signaling Pathway <i>Christopher Breuer, M.D.</i> "Do Tissue Engineered Venous Conduits G Investigating the Growth Potential of Tissu Engineered Venous Conduits in a Juvenile	Grand Sonoran E/F /" Grow? ie Lamb Model″
8:30 – 9:30 a.m.	Journal of Pediatric Surgery Lecture Alberto Peña, M.D. "Luck and Serendipity, the History of a Surgical Technique"	Grand Sonoran E/F
9:30 – 11:15 a.m.	Scientific Session V	Grand Sonoran E/F
11:15 a.m.	Meeting Adjourns	
Noon – 3 p.m.	Executive Council for Pediatric Surgery Organizations	Grand Sonoran H

General Information

Registration

Please note that all authors presenting a paper at the APSA 36th Annual Meeting are required to pay a registration fee.

The onsite registration fees for	the annual meeting are:
APSA Member	\$640
Physician Non-Member	\$740
Student/Resident/Fellow*	\$365
Nurse/Allied * *	\$365
Accompanying Person	\$340

* Students, residents and fellows must have a letter from their chief of service to qualify for the reduced registration fee.

** Registration for the APSA 36th Annual Meeting only; APSNA registration is by separate subscription.

APSA Registration Desk

Registration will be located at the East Registration Desk during the following times:

Saturday, May 28	3 – 6 p.m.
Sunday, May 29	7 a.m. – 5:30 p.m.
Monday, May 30	6:30 a.m. – 1 p.m.
Tuesday, May 31	6:30 a.m. – 1 p.m.
Wednesday, June 1	7:30 – 11:30 a.m.

Scientific Sessions

All educational sessions will be held in the Grand Sonoran E/F. The daily dress code is business or business casual attire.

Poster Viewing

Scientific posters will be located in Grand Sonoran A/B and Grand Sonoran C/D and available for viewing during the following hours:

Sunday, May 29	3:30 – 6 p.m.
Monday, May 30	6:30 a.m. – 1 p.m.
Tuesday, May 31	7 a.m. – 2 p.m.
Wednesday, June 1	7 – 11:15 a.m.
Authors are requested to be in a	ttendance during continent

Authors are requested to be in attendance during continental breakfasts, the reception on Sunday evening and morning breaks to answer audience questions.

Speaker-Ready Room

The speaker-ready room will be available daily, beginning Sunday, May 29, at 7 a.m. in the Grand Canyon 5. Computers will be provided for speakers to review their presentations.

General Information (Continued)

Presentation Check-In

Speakers must use Microsoft PowerPoint[®] slides during their presentations; 35mm slides will not be accepted. Refer to the Guide for Speakers distributed in January and available on the APSA Web site (www.eapsa.org) for information about preparing your presentation. Speakers must submit their computer presentations to the technician in the Speaker-Ready Room (Grand Canyon 5) by 1 p.m. the day before they are scheduled to speak.

Exhibits

Commercial exhibits will be located in the Grand Sonoran Ballroom Foyer and will be open during the following hours:

 Monday, May 30
 6:30 a.m. - 1 p.m.

 Tuesday, May 31
 7 a.m. - 2 p.m.

Continental breakfast and scheduled coffee breaks will be served in the exhibit area on Monday and Tuesday. For a list of exhibitors and booth assignments, see pages A160-A164.

APSA Business Meeting

The APSA Business Meeting will be held from 6:30 – 8 a.m. on Tuesday, May 31, in the Grand Sonoran G meeting room. This is a breakfast meeting and is for APSA members only.

Welcome Reception

A Welcome Reception for all registrants will take place on the Ballroom Lawn from 6:30 – 8:30 p.m. on Sunday, May 29. Tickets for this reception will be included in your registration packet and will be required for admission to the reception. All guests 12 years and older will require a ticket to be admitted to the Welcome Reception. Casual attire is appropriate.

President's Banquet

The President's Banquet will be held in the Grand Sonoran E/F Ballroom on Tuesday, May 31. The reception will begin at 6:30 p.m. in the Grand Sonoran Foyer, and dinner will begin at 7:15 p.m. in Grand Sonoran E/F Ballroom, After dinner, you are invited to join us for dancing. Tickets for the reception and banquet are included in your registration packet and will be required for admission. All guests 12 years and older will require a ticket to be admitted to the banquet. Business or cocktail attire is requested.

Child Care Services

A children's recreation program is available throughout your stay, seven days a week, between 9 a.m. and 4 p.m., by contacting Kokopelli Kids, a full-service children's service featuring arts and crafts, garden walks, scavenger hunts, organized games and more. Kokopelli Kids is for young guests ages 4 to 12. The program hours will be extended during APSA's Tuesday evening President's Banquet to 6-11 p.m. If you prefer to use in-room child care, or if you require a caregiver outside of the Kokopelli Kids program hours, contact the JW Marriott Desert Ridge Resort & Spa Vacation Planning Service at 866/348-9600 for assistance.

Reservations must be made by Friday, May 27 to ensure space is available. Complete details about Kokopelli Kids will be mailed to you with your meeting confirmation. For more information, visit www.jwdesertridgeresort.com or call 480/293-3890.

Companions' Hospitality Suite

The hospitality suite, Suite 2445, will be open Monday from 9 - 11 a.m., Tuesday from 8 - 10:30 a.m. and Wednesday from 8 - 10:30 a.m. Continental breakfast will be served each morning for registered accompanying guests. Badges are requested for entry to the hospitality suite.

Optional Dining Shuttle: Monday, May 30, 6 – 11 p.m.

Though the annual meeting schedule includes special networking events most evenings, Monday night is open for attendees to enjoy the Phoenix/Scottsdale area. APSA has arranged roundtrip coach bus transportation to one of the hot spots of the area — Kierland Commons. The roundtrip transfer fee is \$25 U.S., per person. Due to the Memorial Day holiday, APSA recommends that you make restaurant reservations early by contacting the JW Marriott Desert Ridge Resort & Spa Vacation Planning Service at 866/348-9600. The resort's planning service will be able to provide you restaurant listings and assist with dinner reservations.

Companions Event: Sonoran Desert Hummer Tour — \$125 U.S. per person

The tour will leave the hotel at 8 a.m., Tuesday, May 31, from the Grand Ballroom entrance of the hotel. This is a four-hour guided tour and is appropriate for ages 4 and older. Closed-toe shoes are required and individual waivers must be signed before the activity. Participants will return in time for the Presidential Address. The tour requires a minimum attendance. In the unlikely event of low participation, tour fees will be refunded.

Optional Event: Cattle Drive — \$215 U.S. per person

The tour will leave the hotel at 3:15 p.m. on Monday, May 30, from the Grand Ballroom entrance of the hotel. Experience one of the few remaining traditions of the Old West! Return with your colleagues to the thrilling days of yesteryear by saddling up for a cattle drive. This fun-filled afternoon includes transportation to Bumble Bee Ranch, instructions on horseback riding, a 1¹/₂ hour drive through some of the prettiest parts of the Sonoran Desert, target shooting and a ribeye and chicken dinner (vegetarian dinners available upon request). Ages 10 and older are welcome. The weight maximum for this event is 300 pounds. The tour requires a minimum attendance of 30 people. In the unlikely event of low participation, tour fees will be refunded.

Optional Athletic Activities

The Annual 5K Fun Run will be on Monday, May 30, at 6 a.m. Sign-in will begin at 5:15 a.m. with an organized warm up and stretch at 5:40 a.m. The participation fee is \$35 U.S., which includes a Fun Run T-shirt, water stations along the route, a light breakfast after the run and awards in a number of categories.

The 2005 APSA Golf Tournament will be a shotgun start at the Arnold Palmer Signature Course at 2 p.m. on Monday, May 30. The tournament fee is \$115 U.S., per golfer and includes cart, greens fees, a boxed lunch and awards for the top players.

The APSA Annual Tennis Tournament will be round-robin and begins at 2 p.m., Monday, May 30, at the JW Marriott Desert Ridge Resort & Spa tennis center. The tournament fee is \$35 U.S., per player and includes light refreshments and awards for the top players.

Messages

A message board will be maintained in the registration area during registration hours. Check the board frequently, as there will be NO PAGING during the meeting. To contact the message center, dial the hotel operator or 480/293-5050 and request the APSA Registration Desk.

Guidelines for Authors and Discussants

1. Authors presenting papers are reminded that the presentations shall be limited to six minutes and three minutes (as indicated) for case presentations.

2. Computer disks and CD-ROMs must be turned in to the technician in the Speaker-Ready Room by 1 p.m. the day before they are to be presented.

3. Posters: Please note that the poster session format has changed this year. There will be two poster sessions, both of which will be presented in "walk rounds" format. Scientific posters should be set up Sunday afternoon from 12:30 – 2:30 p.m. and presenters must be available with their posters on Sunday between 4:30 and 6 p.m. to participate in the poster sessions. In addition, authors are asked to be in attendance during the morning refreshment breaks to discuss their presentations. All poster displays must be dismantled on Wednesday, immediately following the annual meeting.

4. Discussants from the floor should state their name and affiliation prior to their remarks. The discussions will be audio recorded for transcription at a later date.

5. Typed discussion should be limited to a maximum of 200 words. Typed discussions that exceed 200 words will be edited before they are submitted to the *Journal of Pediatric Surgery* for publication.

6. Discussants will have the opportunity to edit a transcript of their remarks following the meeting. The Publications Committee reserves the right to edit the typed discussion before it is submitted to the *Journal of Pediatric Surgery*.

The American Pediatric Surgical Association Foundation would like to thank the following APSA members who have contributed to the Foundation. The list is up-to-date as of March 1, 2005.

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Past APSA Annual Meeting Dates and Locations

35th Annual Meeting May 27–30, 2004 Sawgrass Marriott Resort Ponte Vedra Beach, Florida

34th Annual Meeting May 25–28, 2003 Marriott Harbor Beach Resort & Spa Ft. Lauderdale, Florida

33rd Annual Meeting May 19–22, 2002 The Arizona Biltmore Resort and Spa Phoenix, Arizona

32nd Annual Meeting May 20–23, 2001 The Registry Resort Naples, Florida

31st Annual Meeting May 25–28, 2000 Walt Disney World Swan Lake Buena Vista, Florida

30th Annual Meeting May 16–19, 1999 Westin Mission Hills Rancho Mirage, California

29th Annual Meeting May 10–13, 1998 The Hyatt Regency Hilton Head, South Carolina 28th Annual Meeting May 18–21, 1997 The Registry Resort Naples, Florida

27th Annual Meeting May 19–22, 1996 The Hyatt Regency San Diego, California

26th Annual Meeting May 20–23, 1995 The Boca Raton Resort and Club Boca Raton, Florida

25th Annual Meeting May 14–17, 1994 Loews Ventana Canyon Resort Tucson, Arizona

24th Annual Meeting May 15–18, 1993 The Hyatt Regency Hilton Head, South Carolina

23rd Annual Meeting May 12–16, 1992 The Broadmoor Colorado Springs, Colorado

Invited Speakers

Past Annual Meeting Robert E. Gross Lecturers (1990 – 2004)

2004 Giulio (Dan) D'Angio "The Role of the Surgeon in the Past, Present and Future of Pediatric Oncology"

2003 Lucien Leape, M.D. "Safe Health Care — Are We Up to It?"

2002 Harold Shapiro, Ph.D. "The Ethical Dimensions of Scientific Progress"

2001 Judah Folkman, M.D. "Angiogenesis-Dependent Diseases"

2000

J. Bruce Beckwith, M.D. "Pediatric Renal Tumors at the New Millennium: Myths, Misunderstandings, Controversies and Opportunities"

1999 Samuel A. Wells, Jr., M.D. (Title not available)

1998 Richard M. Satava, M.D. "Medicine in the 21st Century"

1997

Douglas W. Wilmore, M.D. "Will Organ Growth Replace Transplantation? Lessons from Patients with Short Bowel Syndrome"

1996 Robert H. Bartlett, M.D. "Surgery, Science and Respiratory Failure"

1995

David A. Williams, M.D. "The Role of Interleukin-II on the Pathophysiology of the Small Intestine"

1994 W. French Anderson, Ph.D. "Human Gene Therapy"

1993 M. Judah Folkman, M.D. "Clinical Applications of Angiogenesis Research"

1992 Warren Zapol, M.D. "Inhaled Nitric Oxide: A Selective Vaso-Dilator"

1991 Joel Cooper, M.D. "History and Current Status of Lung Transplantation"

1990 Richard Simmons, M.D. "Role of the Gut Flora in Surgery"

Past Annual Meeting Overseas/International Guest Lecturers (1990 – 2004)

2004 David A. Lloyd, M.D., FRCS "Tomorrow's Surgeons: Who Cares for the Patient?"

2003 Claire Nihoul-Fékété, M.D. "Modern Surgical Management of Congenital Hyperinsulinemic Hypoglycemia"

2002 Takeshi Miyano, M.D. "Biliary Tree: A Gardener's 30-Year Experience"

Invited Speakers (Continued)

2001

Pedro Rosselló, M.D. "One Nation, with Liberty and Justice...and Healthcare for All"

2000

Leela Kapila, FRCS "Are These the Children of a Lesser God?"

1999

Bernardo Ochoa, M.D. "Pediatric Surgery in Latin America"

1998

Prof. Sidney Cywes "Some of the Little Things We Do — Something Old, Something New"

1997

Justin Kelly "Bladder Exstrophy — Problems and Solutions"

1996

Prem Puri "Variant Hirschsprug's Disease"

1995

Sir Lewis Spitz, M.D., Ph.D., FRCS "Esophageal Atresia — Past, Present and Future"

1994

Sean J. Corkery, M.D.h, FRCSI, FRCSEng "In Pursuit of the Testis"

1993

Edward M. Kiely, FRCSI, FRCS "The Surgical Challenge of Neuroblastoma"

1992

Yann Revillon, M.D. "Intestinal Transplantation in France"

1991

Shemuel Nissan, M.D.

"The History of Surgery and Medicine in the Holy Land from the 19th Century"

1990

Jan C. Molenaar, M.D. "Congenital Diaphragmatic Hernia — What Defect?"

Past Annual Meeting Journal of Pediatric Surgery Lecturers (2001 – 2004)

2004

R. Scott Jones, M.D. "The American College of Surgeons Initiatives for Safety and Quality Improvement"

2003 Patricia Donahoe, M.D. "Sustained Inquiry and Perseverance in the Clinic and at the Bench"

2002 Michael Harrison, M.D. "Fetal Surgery: Trials, Tribulations and Territory"

2001 Joseph P. Vacanti, M.D. "The History and Current Status of Tissue Engineering"

2005 Invited Speakers



Robert E. Gross Lecutre: W. Hardy Hendren, M.D. "Looking Back 50 Years"

W. Hardy Hendren, III, is chief of surgery emeritus at Children's Hospital, Robert E. Gross Distinguished Professor of Surgery at Harvard Medical School, and Honorary Surgeon at Massachusetts General Hospital (MGH). Born in New Orleans in 1926, his family moved to Kansas City in 1933. He graduated from Woodberry Forest School in Virginia in 1943 and enlisted in the U.S. Navy to become a naval aviator. He flew in

the reserves until 1955. When discharged in 1946, he met and married Eleanor, his wife of 58 years.

Dr. Hendren graduated from Dartmouth College in 1948, and from Harvard Medical School in 1952. At Harvard, he helped launch the Internship Matching Plan. He did his residency from 1952 to 1960 in general, thoracic and pediatric surgery at MGH and Children's. In 1960, he founded pediatric surgery at MGH. He became professor of surgery in 1974. He recruited Bruce Henderson, Sam Kim and Patricia Donahoe. Many clinical and laboratory advances followed. He returned in 1982 to Children's as Chief of Surgery and was the first Robert E. Gross Professor in 1985. Considered a master surgeon, Dr. Hendren pioneered major contributions in general and urologic pediatric surgery. He also mentored many surgeons from America and abroad.

Dr. Hendren's awards include: the Ladd Medal from the AAP, the Denis Browne Medal from BAPS, the Urology Medal from the AAP, the Valentine Medal from NY Academy of Medicine and the Bigelow Medal from Boston Surgical. Honorary memberships include the Royal College of Surgeons in Ireland, England and Glasgow. He also received a Certificate of Achievement from the AUA for treatment of urologic disease in children.

Dr. Hendren has served as the President of NESS, APSA, Boston Surgical, Genitourinary Reconstructive Surgeons. He has been the Chairman of the Surgical Section of the AAP and the Vice-President of the ACS. He has published more than 200 papers and 98 book chapters. He has received honorary degrees from the University d'Aix in Marseilles and from Drexel University. He has been the visiting professor at 77 academic centers, equally divided between America and abroad and has operated in 58 of them.

Dr. and Mrs. Hendren raised five children (a nurse, three surgeons and a lawyer) and have 11 grandchildren. Dr. Hendren's greatest joys have been his family and pediatric surgery.

2005 Invited Speakers (Continued)



International Guest Lecture: Prof. Frans W.J. Hazebroek, M.D., Ph.D. "Is Continuation of Life Support Always the Best Option for the Surgical Neonate?"

Frans Hazebroek is chief of the department of pediatric surgery in the Erasmus MC – Sophia Children's Hospital in the Netherlands. In this capacity, he is also chair of the pediatric surgical group, a collaboration of all surgical disciplines in this hospital. Born in The Hague in 1943, he

obtained his medical degree at Leiden University in 1969. After his specialist training in general surgery, he trained in pediatric surgery in Amsterdam and Rotterdam under Professors Anton Vos and Jan Molenaar, respectively. In 1979 he joined the department of pediatric surgery at the Sophia Children's University Hospital, and, in 1998, succeeded Professor Jan Molenaar as professor of pediatric surgery and chief. His main areas of interest lie in the medical ethical aspects of neonatal surgery and the diagnosis and long-term follow up of cryptorchidism and ambiguous genitalia.

In 1987 Dr. Hazebroek obtained a Ph.D. from Erasmus University Rotterdam for his clinical studies on the treatment of cryptorchidism. A recently initiated follow-up study investigates the long-term effects in those prepuberal boys, who have now reached adulthood. He has a long-standing interest in medical ethics and quality of life issues relating to surgery in neonates with life-threatening conditions. His list of publications bears witness to these interests, as does the fact that he served on the boards of various ethics committees, both nationally and locally. In 2003, the European Board of Pediatric Surgery certified the department's pediatric surgical training program, of which Dr. Hazebroek is the director.



Journal of Pediatric Surgery Lecture: Alberto Peña, M.D. "Luck and Serendipity, the History of a Surgical Technique"

Dr. Peña was born and grew up in Mexico City. He attended medical school at the Military Medical School in Mexico City from 1957-1962 and, while there, he achieve the rank of Major. He obtained his surgical training at the Central Military Hospital from 1963-1968.

Dr. Peña became a research fellow at Children's Hospital Medical Center in Boston in 1969 and served as a pediatric surgical resident at the same institution from 1970-1971 where he trained with Robert E.

Gross and M. Judah Folkman. Subsequently, he was appointed surgeon-in-chief at National Institute of Pediatrics in Mexico City and professor of surgery at the University of Mexico. He remained there until June 1985.

In 1985, Dr. Peña was recruited to Long Island, New York, to become chief of pediatric surgery at Schneider Children's Hospital, Northshore Long Island Jewish Health System, where he has remained. He was also professor of surgery at Stony Brook University and, subsequently, professor of surgery and pediatrics at Albert Einstein College of Medicine. As of June 1, 2005, Dr. Peña will be moving to Cincinatti Children's Hospital to direct the New International Center for Pediatric Colorectal and Genitourinary Surgery.

Dr. Peña is married, has four children and eight grandchildren.

2005 Invited Speakers (Continued)

International Pediatric Surgery Panelists

In addition to Professor Hazebroek, Professor George G. Youngson will be joining us on this panel.



Professor George G. Youngson

Professor Youngson is a native Scot who graduated from Aberdeen University Medical School in 1973. After a period of research within Aberdeen and Sweden and completing his basic surgical training within the North of Scotland, he graduated FRCS from the College of Surgeons of Edinburgh in 1977 and Ph.D. from Aberdeen University in 1979. Following completion of certification in general and vascular surgery, during which time he worked in Scotland and London Ontario, he completed his pediatric surgical training in Aberdeen and the

Hospital for Sick Children in Toronto. He was appointed to the position of consultant paediatric surgeon at Royal Aberdeen Children's Hospital in 1984 (succeeding Professor Peter F. Jones) and to a personal chair at the University of Aberdeen in 1999.

His main interests, in addition to clinical surgery, are in strategic health care planning, working for the Department of Health in Scotland, and in surgical education.

He is currently chairman of the examination board in pediatric surgery for the UK colleges, and member of the Specialist Advisory Committee in pediatric surgical training for the UK. He is advisor in pediatric surgery to the chief medical officer in Scotland, and as chairman of the Scottish Colleges Committee on Children's Surgical Services, he represents all surgical disciplines treating children within the Royal Scottish Colleges.

He is married to Sandie, an artist, and their family spans the globe, with children and grandchildren in Auckland, New Zealand, and Manhattan, New York.

PROGRAM IN DETAIL

Friday, May 27

Noon – 9 p.m. Pediatric Surgery Training Directors meeting *Grand Canyon 9/10*

Saturday, May 28

9 a.m. – 5 p.m.	APSA Board of Governors meeting	Desert Conference Suite II
1 – 5 p.m.	Committee meetings	Grand Sonoran H, I, J, K
3 – 6 p.m.	Registration open	East Registration Desk
6 – 10 p.m.	Publications committee meeting/dinner	Desert Conference Suite IV
6:30 – 10 p.m.	APSA Board of Governors dinner	Roy's Restaurant

Sunday, May	29	
6:30 – 8 a.m.	Committee meetings	Grand Sonoran H, I, J, K Desert Conference Suites IV & VI
7 a.m. – 5:30 p.m.	Registration open	East Registration Desk
8 – 10:30 a.m.	Symposium: Bariatric Surgery	Grand Sonoran E/F

Moderator:

• Keith T. Oldham, M.D., Children's Hospital of Wisconsin, Milwaukee, WI

Instructors:

- Carroll M. (Mac) Harmon, M.D., Children's Hospital of Alabama, Birmingham, AL*
- William Dietz, M.D., Centers for Disease Control, Atlanta, GA
- Thomas H. Inge, M.D., Cincinnati Children's Hospital Medical Center, Cincinnati, OH
- Thomas T. Sato, M.D., Children's Hospital of Wisconsin, Milwaukee, WI
- Michael Helmrath, M.D., Texas Children's Hospital Clinical Care Center, Houston, TX
- Walter J. Pories, M.D., FACS, Professor of Surgery and Biochemistry, Brody School of Medicine, East Carolina University, Greenville, NC

*Dr. Harmon is a consultant for Stryker Endoscopy.

Educational Objectives:

- Obtain a basic understanding of the epidemiology, the genetic basis and the physiological impact of adolescent obesity.
- Review the practical organizational aspects of establishing a multidisciplinary pediatric/adolescent program in obesity care and bariatric surgery.
- Be familiar with contemporary published data on adolescent bariatric surgery, particularly Roux Y gastric bypass and gastric restrictive procedures, as well as relevant outcomes.
- Understand similarities and differences in the management of bariatric surgical patients in adult and pediatric or adolescent age groups.

Genetic and Physiological Basis for Obesity Carroll M. (Mac) Harmon, M.D.

Epidemiology and Medical Aspects William Dietz, M.D.

Organization & Program Development Thomas H. Inge, M.D.

Surgical Management Thomas T. Sato, M.D. Michael Helmrath, M.D.

Adult Bariatric Surgery Walter J. Pories, M.D., FACS

10:30 – 11 a.m.	Refreshment break	Grand Sonoran Foyer
11 a.m. – Noon	International Surgical Education Panel	Grand Sonoran E/F

Moderator:

• Diana L. Farmer, M.D., University of California-San Francisco, San Francisco, CA

Panelists:

- Professor George G. Youngson, M.D., Royal Aberdeen Children's Hospital, Aberdeen, Scotland, United Kingdom
- Professor Frans W.J. Hazebroek, M.D., Ph.D., Sophia Children's Hospital, Rotterdam, The Netherlands

12:30 – 1:30 p.m.	Lunch with video session	Grand Sonoran E/F

Moderators:

- Edward M.Barksdale, Jr., M.D.
- Daniel H. Teitelbaum, M.D.

Educational Objectives:

The video session will update the participants on clinical problems in pediatric surgery.

V1 USE OF THE STRETTA PROCEDURE FOR RADIOFREQUENCY ABLATION OF THE LOWER ESOPHAGEAL SPHINCHTER IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE*

<u>Ariel U. Spencer, M.D.¹</u>, Donald C. Liu, M.D.,Ph.D.², Daniel H. Teitelbaum, M.D.¹, ¹University of Michigan, Ann Arbor, MI, U.S.A., ²University of Chicago, Chicago, IL, U.S.A.

*Author will discuss the Stretta Procedure as an investigational use in pediatric patients.

V2 MODIFIED NUSS PROCEDURE:

TECHNIQUES FOR ASYMMETRIC PECTUS EXCAVATUM <u>Hyung Joo Park, M.D.</u>, Seung Jin Lee, M.D., Seock Yeol Lee, M.D., Cheol Sae Lee, M.D., Soonchunhyang University Chunan Hospital, Chunan, Republic of Korea

Underlining denotes the author scheduled to present at the meeting.

- V3 VIDEO-ASSISTED THORACOSCOPIC SURGICAL EXCISION OF A RIGHT UPPER LOBE CPAM <u>Curt S. Koontz, M.D.</u>, Kenneth Gow, M.D., Mark L. Wulkan, M.D., Emory University School of Medicine, Atlanta, GA, U.S.A.
- V4 MINIMALLY INVASIVE THORACOSCOPIC ULTRASOUND (MITUS) FOR RESECTION OF PULMONARY NODULES <u>Kenneth W. Gow, M.D.</u>, Mark L. Wulkan, M.D., Emory University, Atlanta, GA, U.S.A.
- V5 ROBOTIC EXCISION OF CHOLDOCHAL CYST James D. Geiger, M.D., Oliver S. Soldes, M.D., University of Michigan, Ann Arbor, MI, U.S.A.
- V6 LAPAROSCOPIC HEPATOPORTO-ENTEROSTOMY (KASAI PROCEDURE) <u>Hanmin Lee, M.D.</u>¹, Matthew S. Clifton, M.D.², Michael Harrison, M.D.³, Kerilyn Nobuhar, M.D.³, Erich Grethel, M.D.³, Raul Cortes, M.D.³, Diana Farmer, M.D.³, ¹University of California (Division of Pediatrics), San Francisco, CA, U.S.A., ²University of California (Divison of Pediatric Surgery), San Francisco, CA, U.S.A., ³University of California (Division of Pediatric Surgery), San Francisco, CA, U.S.A.

12:30 – 2:30 p.m.	Poster Set-up	Grand Sonoran A/B
		Grand Sonoran C/D
2 – 4:30 p.m.	Symposium: Endoscopic Surgery	Grand Sonoran E/F

Instructors:

- Michael G. Caty, M.D., Buffalo Children's Hospital, Buffalo, NY
- W. Raleigh Thompson, M.D., University of Miami School of Medicine, Miami, FL
- Hanmin Lee, M.D., University of California at San Francisco Fetal Treatment Center, San Francisco, CA

Educational Objectives:

Attend this session to learn about the newest endoscopic surgery techniques and new ways to treat patients using the least-invasive methods. We will discuss what those newest to our field have to say about endoscopic surgery and about complications that can result from these techniques.

Current Practice of Pediatric Surgery Michael G. Caty, M.D.

Complications of Pediatric Endosurgery W. Raleigh Thompson, M.D.

Neonatal Endosurgery Hanmin Lee, M.D.

The Private Perspective Panel Poster Sessions (two parallel and concurrent sessions)

4:30 – 5:15 p.m.

Poster Session 1A: Hematology and Oncology

Moderator:

• Edward M. Barksdale, Jr., M.D.

Educational Objectives:

- Understand some of the immune-related responses to childhood tumors.
- Appreciate the factors expressed by and signals mediated in response to childhood tumors.
- Familiarize one with some of the new or potential therapeutic options which may be used to treat childhood tumors.
- P1 STRUCTURAL ANALYSIS OF THE HUMAN NEUROBLASTOMA DNA REPLICATION COMPLEX: INSIGHTS INTO FAULTY PROLIFERATION John A. Sandoval, M.D., Jay L. Grosfeld, M.D., Robert J. Hickey, Ph.D., Linda H. Malkas, Ph.D., Indiana University School of Medicine, Indianapolis, IN, U.S.A.
- P2 MIS INHIBITS TUMOR GROWTH IN VIVO IN A NEW ANIMAL MODEL, WHICH RECAPITULATES HUMAN OVARIAN CANCER <u>Rafael Pieretti-Vanmarcke, M.D.¹, David T. MacLaughlin, Ph.D.¹, Denise Connolly, Ph.D.², Patricia K. Donahoe, M.D.¹, ¹Massachusetts General Hospital, Boston, MA, U.S.A., ²Fox Chase Cancer Center, Philadelphia, PA, U.S.A.</u>
- P3 REGULATORY EFFECT OF NERVE GROWTH FACTOR ON THE ERK1 PATHWAY IN WILD-TYPE, DOXORUBICIN-RESISTANT, AND NERVE GROWTH FACTOR-TRANSFECTED NEUROBLASTOMA CELL LINES <u>Bill Chiu, M.D.</u>, Bernard Mirkin, Ph.D., M.D., Robert Arensman, M.D., Mary Beth Madonna, M.D., Children's Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL, U.S.A.
- P4 DIFFERENTIAL SIGNALING RESPONSE OF NEUROBLASTOMA TO MEK ACTIVITY INHIBITOR TREATMENT PREDICTS RESISTANCE TO MAP KINASE BASED TREATMENT STRATEGIES <u>Andrew C. Eppstein, M.D.</u>, John A. Sandoval, M.D., Patrick J. Klein, Ph.D., Heather A. Woodruff, B.S., Jay L. Grosfeld, M.D., Robert J. Hickey, Ph.D., Linda H. Malkas, Ph.D., Christian M. Schmidt, M.D., Ph.D., Indiana University School of Medicine, Indianapolis, IN, U.S.A.
- P5 INDUCTION OF IMMUNE RESPONSES TO, AND IDENTIFICATION OF, SHARED TUMOR ASSOCIATED ANTIGENS IN RHABDOMYOSARCOMA <u>David A. Rodeberg, M.D.</u>, Courtney Erskine, B.S., Esteban Celis, M.D., Mayo Foundation, Rochester, MN, U.S.A.
- P6 NEUROBLASTOMA IMPAIRS CHEMOKINE-MEDIATED DENDRITIC CELL MIGRATION IN VITRO Sonya R. Walker, M.D., <u>P. Dafé Ogagan, B.S.</u>, Alex Aboka, B.S., Edward M. Barksdale, Jr., M.D., FAAP, FACS, Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

Underlining denotes the author scheduled to present at the meeting.

P7 PI3 KINASE MEDIATES BILE SALT INDUCED PROLIFERATION IN A TELOMERASE IMMORTALIZED BARRETT'S CELL LINE

<u>Kshama R. Jaiswal, M.D.</u>¹, Christie Lopez-Guzman, B.S.¹, Fiemu Nwariaku, M.D.¹, Thomas Anthony, M.D.¹, R. Todd Maxson, M.D.², George A. Sarosi, M.D.¹, ¹University of Texas Southwestern and Dallas VAMC, Dallas, TX, U.S.A., ²Children's Medical Center Dallas and University of Texas Southwestern Medical Center, Dallas, TX, U.S.A.

- P8 PHOSPHATIDYLSERINE ON ENDOTHELIUM DERIVED MICROPARTICLES INHIBITS DENDRITIC CELL FUNCTION John C. Densmore, M.D.¹, Xiao Chen, M.D.¹, Kara Doffek¹, Sonia L. Sugg, M.D.², Keith T. Oldham, M.D.¹, Joel Shilyansky, M.D.¹, ¹Children's Hospital of Wisconsin, Milwaukee, WI, U.S.A., ²Medical College of Wisconsin, Milwaukee, WI, U.S.A.
- P9 ETOPOSIDE ENHANCES TRAIL-INDUCED CYTOTOXICITY IN HUMAN OSTEOSARCOMA <u>Debra K. Doherty, M.D.</u>, Jonathan L. Davies, B.S., Eugenie S. Kleinerman, M.D., Anderson Cancer Center, Houston, TX, U.S.A.
- P10 NOVEL PEPTIDES SECRETED FROM HUMAN NEUROBLASTOMA: USEFUL CLINICAL TOOLS? John A. Sandoval, M.D., Derek J. Hoelz, Ph.D., Heather A. Woodruff, B.S., Robert L. Powell, B.S., <u>Colleen L. Jay, B.S.</u>, Jay L. Grosfeld, M.D., Robert J. Hickey, Ph.D., Linda H. Malkas, Ph.D., Indiana University School of Medicine, Indianapolis, IN, U.S.A.
- P11 NEUROBLASTOMAS DO NOT RECUR LOCALLY REGARDLESS OF EXTENT OF TUMOR RESECTION WHEN TREATED WITH THE CHICAGO PILOT II PROTOCOL Marybeth Browne, M.D., Morris Kletzel, M.D., Roopa Seskardi, Susan L. Cohn, M.D., <u>Marleta Reynolds, M.D.</u>, Children's Memorial Hospital, Chicago, IL, U.S.A.

5:15 – 6 p.m. Poster Session 1B: Clinical Surgery Grand Sonoran A/B

Moderator:

• Anthony Stallion, M.D.

Educational Objectives:

- Understand some of the newer approaches to the treatment of pediatric surgical conditions.
- Understand the pathophysiology of various pediatric surgical conditions.
- Appreciate some of the unique variants and aspects of unique pediatric surgical conditions.

P12 PEDIATRIC TRAUMA NURSE PRACTITIONERS PROVIDE EXCELLENT CARE WITH SUPERIOR PATIENT SATISFACTION FOR INJURED CHILDREN <u>Kaaren Fanta, R.N., M.S.N., CPNP</u>, Becky Cook, R.N., M.S.N., CPNP, Crystal Rickets, Ph.D, Lynn Schweer, R.N., M.S.N., CPNP, Richard A. Falcone, Jr., Rebeccah L. Brown, Victor F. Garcia, Cincinnati Children's Hospital Medical Center, Cicinnati, OH, U.S.A.

- P13 SLOW TRANSIT CONSTIPATION-DIAGNOSTIC PITFALLS Shailinder Jit Singh, M.S., DNB, MCh, FRCS I, FRCS (Eng.), FRCS (Paed.Surg.), Professor Alan Perkins, B.Sc. (Hons), M.Sc., Ph.D., Queen's Medical Centre, Nottingham, United Kingdom. WITHDRAWN
- P14 OUTCOME OF LONGITUDINAL PANCREATICOJEJUNOSTOMY FOR CHRONIC PANCREATITIS IN CHILDREN Jaimie D. Nathan, M.D., Henry E. Rice, M.D., Michael A. Skinner, M.D., Duke University Medical Center, Durham, NC, U.S.A.
- P15 COMPLEX PANCREATIC VASCULAR ANOMALIES <u>Adam M. Vogel, M.D.</u>, Julia M. Alesbury, Victor L. Fox, M.D., Steven J. Fishman, M.D., Children's Hospital Boston, Boston, MA, U.S.A.
- P16 PEDIATRIC SHORT BOWEL SYNDROME: WHAT IT ACTUALLY COSTS <u>Ariel U. Spencer, M.D.</u>, Debra Kovacevich, R.N., Deanna Hair, B.A., Michelle McKinney-Barnett, B.S., Christopher Maksym, R.Ph., Daniel H. Teitelbaum, M.D., University of Michigan, Ann Arbor, MI, U.S.A.
- P17 THE EFFECT OF A RIGHT SIDED AORTIC ARCH ON OUTCOME IN CHILDREN WITH ESOPHAGEAL ATRESIA <u>Steven R. Allen, M.D.</u>, Romeo Ignacio, M.D., Richard Falcone, M.D., Maria Alonso, M.D., Frederick Ryckman, M.D., Victor Garcia, M.D., Richard Azizkhan, M.D., Gregory Tiao, M.D., Cincinnati Children's Hospital Medical Center, Cincinnati, OH, U.S.A.
- P18 LAPAROSCOPIC APPENDECTOMY WITH AN UMBILICALLY PLACED DUAL-PURPOSE THORACOSCOPIC INSTRUMENT <u>Felix Schier, M.D.</u>, Salmai Turial, M.D., Alexandra Weltzien, M.D., Veronika Engel, M.D., Cordula Scherer, M.D., Jörg Beardi, M.D., University Medical Centre, Mainz, Germany.
- P19 THE APPENDIX SIGN: A RADIOGRAPHIC MARKER FOR IRREDUCIBLE INTUSSUSCEPTION <u>Marion C. W. Henry, M.D.</u>, Christopher K. Breuer, M.D., David Tashjian, M.D., R. Lawrence Moss, M.D., Milissa McKee, M.D., Robert Touloukian, M.D., T. Rob Goodman, Cindy Miller, Jamal Bokhari, Yale University, New Haven, CT, U.S.A.
- P20 INCIDENCE OF PERSISTENT LEFT SUPERIOR VENA CAVA IN ESOPHAGEAL ATRESIA <u>Nathan Mowery, M.D.</u>, Deborah F. Billmire, M.D., Marcus Shamberger, M.D., Paul Szotek, M.D., Karen West, M.D., Frederick Rescorla, M.D., L. R. Scherer, M.D., Scott Engum, M.D., Tom Rouse, M.D., Jay L. Grosfeld, M.D., Indiana University, Indianapolis, IN, U.S.A.
- P21 THE USE OF ALLODERM[®] IN THE REPAIR OF CEPHALIC FOLD OMPHALOCELE <u>Michael R. Curci, M.D.</u>¹, Albert W. Dibbins, M.D.², Thomas Hamilton, M.D.², Janice Dudley, R.N., PNP², ¹Maine Medical Center, Portland, ME, U.S.A., ²Maine Medical Center, Portland, ME, U.S.A.

Underlining denotes the author scheduled to present at the meeting.

P22 EXTRACELLULAR MATRIX DYNAMICS ASSOCIATED WITH TISSUE-ENGINEERED INTRAVASCULAR SCLEROTHERAPY

Adam M. Vogel, M.D., <u>C. Jason Smithers, M.D.</u>, Harry P. Kozakewich, M.D., David Zurakowski, Ph.D., Marsha A. Moses, Ph.D., Patricia E. Burrows, M.D., Dario O. Fauza, M.D., Steven J. Fishman, M.D., Children's Hospital Boston, Boston, MA, U.S.A.

4:30 – 5:15 p.m. Poster Session 2A: Basic Science

Grand Sonoran C/D

Moderator:

• Ai-Xuan L. Holterman, M.D.

Educational Objectives:

- Understand the etiologies of various pediatric surgical conditions.
- Appreciate some of the embryologic etiologues of pediatric surgical anomalies.
- Appreciate some of the unique signaling mechanisms involved in various pediatric surgical conditions.
- P23 ABSENCE OF TREFOIL FACTOR 2 ACCELERATES INTESTINAL INJURY IN A MOUSE MODEL OF NECROTIZING ENTEROCOLITIS <u>Cynthia A. Gingalewski, M.D.</u>, Robert Kiley, M.D., Robert Finberg, M.D., Rhonda Yantiss, M.D., Evelyn Kurt-Jones, Ph.D., University of Massachusetts, Worcester, MA, U.S.A.
- P24 THE ROLE OF TOLL LIKE RECEPTOR-4 IN THE PATHOGENESIS OF NECROTIZING ENTEROCOLITIS <u>Cynthia L. Leaphart, M.D.</u>, Matthew Rivenburgh, B.S., Matthew D. Neal, B.S., Selma Cetin, M.D., Jun Li, Henri R. Ford, M.D., David J. Hackam, M.D., Ph.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.
- P25 THE INNATE IMMUNE SYSTEM: ONTOGENY OF THE TOLL-LIKE RECEPTOR Cynthia A. Gingalewski, M.D., <u>Robert Kiley, M.D.</u>, Evelyn Kurt-Jones, Ph.D., Robert Finberg, M.D., University of Massachusetts, Worcester, MA, U.S.A.
- P26 EFFECTS OF PEROXYNITRITE ON MAPK ACTIVATION IN ENTEROCYTE APOPTOSIS Lydia Stephenson, B.A., Sarah Steinhauser, B.S., Xiaru Zhang, M.D., Dilhari Delamedia, B.A., Henri R. Ford, M.D., Anatoly Grishin, Ph.D., Jeffrey S. Upperman, M.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.
- P27 NITRIC OXIDE IMPAIRS ENTEROCYTE MIGRATION THROUGH INACTIVATION OF THE SMALL GTP PROTEIN RAC1 <u>Selma Cetin, M.D.</u>, Cynthia Leaphart, M.D., Jun Li, R.N., Henri R. Ford, M.D., David J. Hackam, M.D., Ph.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.
- P28 DISTENSION ENTEROGENESIS: INCREASING INTESTINAL SIZE AND FUNCTION <u>Devin Puapong</u>¹, Benjamin Wu², James Atkinson², James Dunn², ¹Kaiser Permanente, Los Angeles, CA, U.S.A., ²University of California Los Angeles, Los Angeles, CA, U.S.A.

Underlining denotes the author scheduled to present at the meeting.

Final Program

- P29 ONTOGENY OF SODIUM-GLUCOSE CO-TRANSPORTER-1 (SGLT-1) IN A FETAL RABBIT MODEL OF INTRAUTERINE GROWTH RETARDATION (IUGR) <u>Christina Cellini, M.D.</u>, Jian Xu, M.D., Terry L. Buchmiller-Crair, M.D., Children's Hospital of NY Presbyterian-Weill Cornell Medical College, New York, NY, U.S.A.
- P30 NF-kB NEGATIVELY REGULATES LIPOPOLYSACCHARIDE SIGNALING IN ENTEROCYTES VIA INDUCTION OF MKP1 PHOSPHATASE <u>Anatoly V. Grishin, Ph.D.</u>, Jin Wang, M.S., Athalie Young, David J. Hackam, M.D., Ph.D., Jeffrey Upperman, M.D., Ruben Zamora, Ph.D., Henri R. Ford, M.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.
- P31 HEPATIC OVAL CELLS AND WNT SIGNALING <u>Masashi Kurobe</u>, Yue Xu, Brett Staahl, Roel Nusse, Karl G. Sylvester, M.D., Stanford University, Stanford, CA, U.S.A.
- P32 ANORECTAL MALFORMATION IN EPHRIN-B2^{LACZ/LACZ} MUTANT MICE* <u>Nilda M. Garcia, M.D.</u>, M E. Martinez, M.S., C. Dravis, M.S., D. Vasquez, M.D., M. Henkemeyer, Ph.D., Linda Baker, M.D., UT Southwestern Med Center, Dallas, TX, U.S.A.

*Authors received grants/research support from NIH.

5:15 – 6 p.m.	Poster Session 2B: Embryology,	Grand Sonoran C/D
	Fetal Surgery and Tissue Engineering	

Moderator:

• Daniel H. Teitelbaum, M.D.

Educational Objectives:

- Understand some of the unique factors responsible for the embryogenesis of various organ systems.
- Gain an appreciation for some of the newer prenatal modalities to define pediatric surgical conditions.
- Understand some of the newer techniques in tissue engineering as they relate to pediatric surgical conditions.

P33 NDSP IS A NOVEL NERVE GROWTH FACTOR RESPONSIVE GENE

Sanjeev A. Vasudevan, M.D.¹, Kuan Wang, M.D., Ph.D.², Susan M. Burlingame¹, Jianhua Yang, Ph.D.², Jed G. Nuchtern, M.D.³, ¹M.E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, U.S.A., ²Texas Children's Cancer Center, Department of Pediatrics, Baylor College of Medicine, Houston, TX, U.S.A., ³M.E. DeBakey Department of Surgery, Texas Children's Cancer Center, Department of Pediatrics, Baylor College of Medicine, Young, TX, U.S.A.

P34 THREE DIMENSIONAL COMPUTERIZED THORACIC VOLUME RECONSTRUCTION FROM TWO DIMENSIONAL RADIOGRAPHS: A NEW TECHNIQUE FOR CDH PATIENTS

*Erich J. Grethel, M.D.*¹, Sohrab Gollogly, M.D.², Roberta L. Keller, M.D.¹, Catherine Logan, B.S.², Amy J. Wagner, M.D.¹, Matthew S. Clifton, M.D.¹, Raul A. Cortes, M.D.¹, Hanmin Lee, M.D.¹, Diana Farmer, M.D.¹, Michael R. Harrison, M.D.¹, Kerilyn K. Nobuhara, M.D.¹, ¹University of California-San Francisco, San Francisco, CA, U.S.A., ²Orthopedics, Scoliosis, and Spine Surgery, Monterey, CA, U.S.A.

- P35 MR SPECTROSCOPY FOR EVALUATING FETAL LUNG MATURITY <u>Matthew S. Clifton, M.D.</u>, Bonnie N. Joe, M.D., Ph.D., Mark Swanson, Ph.D., Andrew Zektzer, Ph.D., John Kurhanewicz, Ph.D., Daniel B. Vigneron, Ph.D., Fergus Coakley, M.D., Robert Ball, M.D., Amy J. Wagner, M.D., Raul A. Cortes, M.D., Erich J. Grethel, M.D., Vickie Feldstein, M.D., Kerilyn K. Nobuhara, M.D., University of California, San Francisco, San Francisco, CA, U.S.A.
- P36 HISTOLOGICAL EVIDENCE OF VENOUS OBSTRUCTION IN FETAL EXTRALOBAR PULMONARY SEQUESTRATION ASSOCIATED WITH TENSION HYDROTHORAX <u>Yoshihiro Kitano, M.D.</u>, Toshiro Honna, M.D., Tatsuo Kuroda, M.D., Nobuyuki Morikawa, M.D., Kentarou Matsuoka, M.D., Satoshi Hayashi, M.D., Haruhiko Sago, M.D., National Center for Child Health and Development, Setagaya-ku, Japan.
- P37 TRACHEAL OCCLUSION IN FETAL RATS ALTERS EXPRESSION OF MESENCHYMAL NUCLEAR TRANSCRIPTION FACTORS WITHOUT AFFECTING SURFACTANT PROTEIN EXPRESSION <u>Enrico Danzer, M.D.</u>¹, Lauren E. Robinson¹, Marcus G. Davey, Ph.D.¹, Uwe Schwarz, M.D.¹, MaryAnn Volpe, M.D.², N. Scott Adzick, M.D.¹, Alan W. Flake, M.D.¹, Holly L. Hedrick, M.D.¹, ¹The Children's Hospital of Philadelphia, Philadelphia, PA, U.S.A., ²New England Medical Center, Boston, MA, U.S.A.
- P38 EFFECT OF VEGF ON THE BRANCHING MORPHOGENESIS OF NORMAL AND NITROFEN-INDUCED HYPOPLASTIC FETAL RAT LUNG EXPLANTS <u>Masato Shinkai, M.D.</u>, Toko Shinkai, M.D., Sandra Montedonico, M.D., Prem Puri, M.S., FRCS, Children's Research Centre, Our Lady's Hospital for Sick Children, Dublin, Ireland.
- P39 GENE EXPRESSION PROFILE OF THE WNT FAMILY IN CRANIAL SUTURE DEVELOPMENT <u>Preeti Malladi, M.D.</u>, Yue Xu, M.D., Ph.D., Roel Nusse, Ph.D., Michael T. Longaker, M.D., M.B.A., Stanford University, Stanford, CA, U.S.A.
- P40 CARTILAGE ENGINEERING FROM MESENCHYMAL AMNIOCYTES: POSSIBLE APPLICATION IN THE TREATMENT OF CONGENITAL TRACHEAL ANOMALIES <u>Shaun M. Kunisaki, M.D.</u>, M.Sc., Russell W. Jennings, M.D., Dario O. Fauza, M.D., Children's Hospital Boston, Boston, MA, U.S.A.

Underlining denotes the author scheduled to present at the meeting.
Sunday, May 29 (Continued)

- P41 TISSUE ENGINEERING OF THE ADRENAL CORTEX James C.Y. Dunn, M.D., Ph.D., Yinting Chu, Julianne M. Mendoza, M.D., James B. Atkinson, M.D., Edward RB McCabe, M.D., Ph.D., UCLA, Los Angeles, CA, U.S.A.
- P42 DEVELOPMENT OF A MODEL SYSTEM FOR PRELIMINARY EVALUATION OF TISSUE ENGINEERED VASCULAR CONDUITS <u>Amit Goyal</u>, Yinong Wang, Haili Su, Lawrence W. Dobrucki, Matthew Brennan, Peter Fong, Alan Dardik, George Tellides, Jordan Pober, W. Mark Saltzman, M.D., Ph.D., Christopher K. Breuer, M.D., Yale University, New Haven, CT, U.S.A.
- P43 GENE TRANSFER OF PIGMENT EPITHELIUM-DERIVED FACTOR SUPPRESSES TUMOR GROWTH AND ANGIOGENESIS IN EXPERIMENTAL HEPATOBLASTOMA <u>Marybeth Browne, M.D.</u>¹, Veronica Stellmach, Ph.D.², Mona Cornwell², Eun Jig Lee, M.D.², Lisa P. Abramson, M.D.¹, Riccardo A. Superina, M.D.¹, Marleta Reynolds, M.D.¹, Susan E. Crawford, M.D.², ¹Children's Memorial Hospital, Chicago, IL, U.S.A., ²Feinberg School of Medicine, Northwestern University, Chicago, IL, U.S.A.
- P44 GENERATION OF THE FIRST TRANSGENIC MOUSE EXPRESSING AN ENDOTHELIAL MARKER

Angela V. Kadenhe-Chiweshe, M.D., <u>Jae-O Bae, M.D.</u>, Paivi Ullner, M.D., Elizabeth Ferrari, B.S., Sulli Popilskis, D.V.M., Darrell Yamashiro, M.D., Jessica Kandel, M.D., Columbia University, New York, NY, U.S.A.

5:30 – 6:30 p.m.	Exhibit set-up	Grand Sonoran Foyer
6:30 – 8:30 p.m.	Welcome Reception	Ballroom Lawn

Monday, May 30

6 – 7:30 a.m.	Annual 5K Fun Run	Grand Ballroom Entrance
6:30 – 7:30 a.m.	Committee meetings	Grand Sonoran H, I, J, K
	Conter	ence Desert Sultes IV & VI
6:30 a.m. – 1 p.m.	Registration open	East Registration Desk
6:30 a.m. – 1 p.m.	Exhibits open; poster viewing	Grand Sonoran A/B; C/D Foyer
6:30 – 7:30 a.m.	Continental breakfast in the exhibits area	Grand Sonoran Foyer
7:30 – 9:15 a.m.	Welcome/Scientific Session I: Diaphragmatic Hernia and Thoracic D	Grand Sonoran E/F Diseases

Moderators:

- Wallace W. Neblett, III, M.D.
- Terri L. Buchmiller, M.D.

Educational Objectives:

The participants in this session will be provided with contemporary insights on and long-term outcomes for the management of congenital diaphragmatic hernia and other pediatric thoracic surgical conditions.

- BIRTHWEIGHT AND MCGOON INDEX PREDICT SEVERITY IN NEWBORN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH) (6 MINUTES) <u>Germana Casaccia, M.D.</u>, F. Crescenzi, M.D., A. Dotta, M.D., I. Capolupo, M.D., A. Braguglia, M.D., O. Danhaive, M.D., L. Pasquini, M. Bevilacqua, M.D., Pietro Bagolan, M.D., M. Orzalesi, M.D., C. Corchia, M.D., Pediatric Hospital Bambino Gesù, Rome, Italy.
- 2 PROSTHETIC PATCHES FOR CONGENITAL DIAPHRAGMATIC HERNIA REPAIR: SURGISIS[®] VERSUS GORE-TEX[®] (3 MINUTES) <u>Erich J. Grethel, M.D.</u>, Raul A. Cortes, M.D., Amy J. Wagner, M.D., Matthew S. Clifton, M.D., Tiffany C. Townsend, M.D., Hanmin Lee, M.D., Diana L. Farmer, M.D., Michael R. Harrison, M.D., Roberta L. Keller, M.D., Kerilyn K. Nobuhara, M.D., University of California, San Francisco, CA, U.S.A.
- 3 EFFECTS OF SURGICAL REPAIR OF CONGENITAL DIAPHRAGMATIC HERNIA (CDH) ON CEREBRAL HAEMODYNAMICS EVALUATED BY NEAR INFRARED SPECTROSCOPY (NIRS)* (3 MINUTES) Andrea Dotta, M.D., Jole Rechichi, M.D., Francesca Campi, M.D., <u>Annabella Braguglia, M.D.</u>, Sabrina Palamides, M.D., Irma Capolupo, M.D., S. Lozzi, M.D., Alessandro Trucchi, Carlo Corchia, M.D., Pietro Bagolan, Marcello Orzalesi, M.D., Pediatric Hospital Bambino Gesù, Rome, Italy. * The authors received a grant from the Italian Ministry of Health.
- 4 DIAPHRAGMATIC REPAIR THROUGH FETAL TISSUE ENGINEERING: A COMPARISON BETWEEN MESENCHYMAL AMNIOCYTE- AND MYOBLAST-BASED CONSTRUCTS (3 MINUTES) <u>Shaun M. Kunisaki, M.D.</u>¹, Julie R. Fuchs, M.D.¹, Amir Kaviani, M.D.¹, Jung-Tak Oh, M.D.¹, David LeVan, Ph.D.², Joseph P. Vacanti, M.D.³, Jay M. Wilson, M.D.¹, Dario O. Fauza, M.D.¹, ¹Children's Hospital Boston, Boston, MA, U.S.A., ²Massachusetts Institute of Technology, Boston, MA, U.S.A., ³Massachusetts General Hospital, Boston, MA, U.S.A.
- 5 LUNG VOLUMES AND DISTRIBUTION OF VENTILATION DURING THE FIRST TWO YEARS OF LIFE IN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH)* (3 MINUTES) <u>Andrea Dotta, M.D.</u>, Sabrina Palamides, Annabella Braguglia, Francesco Crescenzi, Germana Casaccia, Anna Maria Guadagni, Maria Paola Ronchetti, Pietro Bagolan, Carlo Corchia, Pediatric Hospital Bambino Gesù, Rome, Italy. * The authors received a grant from the Italian Ministry of Health.

- 6 IS PERICOSTAL BAR FIXATION TECHNIQUE REALLY NECESSARY IN THE NUSS PROCEDURE?; SUBMUSCULAR BAR FIXATION TECHNIQUE (3 MINUTES) <u>Hyun Koo Kim, M.D., Ph.D.,</u> Young Ho Choi, M.D., Ph.D., Yang Hyun Cho, M.D., Se Min Ryu, M.D., Young-sang Sohn, M.D., Ph.D., Hark Jei Kim, M.D., Ph.D., Guro Hospital, Korea University Medical Center, Seoul, Republic of Korea.
- 7 NON-OPERATIVE MANAGEMENT OF PECTUS CARINATUM (3 MINUTES) <u>Ala Stanford Frey, M.D.</u>, Greg Durrett, Certified Orthotist, Victor F. Garcia, M.D., Rebeccah L. Brown, M.D., Thomas H. Inge, M.D., Frederick C. Ryckman, M.D., Richard G. Azizkhan, M.D., Cincinnati Children's Hospital Medical Center, Cincinnati, OH, U.S.A.
- 8 USE OF A BIODEGRADABLE PATCH FOR RECONSTRUCTION OF LARGE THORACIC CAGE DEFECTS IN GROWING CHILDREN (6 MINUTES) <u>Melvin D. Smith, M.D.</u>, Robert M. Campbell, University Texas Health Science Center, San Antonio, San Antonio, TX, U.S.A.
- 9 LONG-TERM FOLLOW-UP AFTER THYMECTOMY FOR MYASTHENIA GRAVIS: |THORACOSCOPIC VS. OPEN (3 MINUTES) <u>Amy J. Wagner, M.D.,</u> Raul A. Cortes, M.D., Erich J. Grethel, M.D., Matthew S. Clifton, M.D., Michael R. Harrison, M.D., Diana Farmer, M.D., Kerilyn K. Nobuhara, M.D., Jonathan Strober, M.D., Hanmin Lee, M.D., UCSF, San Francisco, CA, U.S.A.
- 10 ESOPHAGEAL STRICTURES IN CHILDREN WITH EPIDERMOLYSIS BULLOSA: AN 11-YEAR EXPERIENCE WITH FLUOROSCOPY-GUIDED BALLOON DILATATION (3 MINUTES) <u>Wolfgang Stehr, M.D.</u>, Benjamin D. Hammelman, John M. Racadio, M.D., Richard G. Azizkhan, M.D., Cincinnati Children's Hospital, Cincinnati, OH, U.S.A.
- 11 BRONCHIAL ATRESIA: THE HIDDEN PATHOLOGY WITHIN A SPECTRUM OF PRENATALLY DIAGNOSED LUNG MASSES (3 MINUTES) Shaun Kunisaki, M.D., Dario Fauza, Luanne Nemes, RNP, Carol Barnewolt, M.D., Judy Estroff, M.D., Harry Kozakewitch, M.D., <u>Russell Jennings, M.D.</u>, Children's Hospital Boston, Boston, MA, U.S.A.
- 12 PRENATAL DIAGNOSIS AND OUTCOME OF CHILDREN WITH PLEUROPULMONARY BLASTOMA (3 MINUTES) <u>Douglas N. Miniati, M.D.</u>, Murali Chintagumpala, M.D., Claire Langston, M.D., Oluyinka O. Olutoye, M.D., Ph.D., Jed G. Nuchtern, M.D., Darrell L. Cass, M.D., Baylor College of Medicine, Houston, TX, U.S.A.

9:15 – 10:15 a.m.	Robert E. Gross Lecture W. Hardy Hendren, M.D. "Looking Back 50 Years"	Grand Sonoran E/F
10:15 – 10:45 a.m.	Refreshment break	Grand Sonoran A/B, C/D, & Foyer

10:45 a.m. – Noon

Scientific Session II: Trauma and Hepatobiliary Diseases

Moderators:

- Ai-Xuan L. Holterman, M.D.
- Anthony Stallion, M.D.

Educational Objectives:

Presentations in this session will provide the attendee with information regarding emerging concepts in the management and care of the pediatric trauma patient with a particular focus on outcomes. The session will also provide the participant with evolving insights in the management of patients with complex hepatobiliary conditions.

- 13 DIAGNOSTIC AND THERAPEUTIC LAPAROSCOPY IN PEDIATRIC ABDOMINAL TRAUMA (6 MINUTES) <u>Alexander Feliz, M.D.</u>, Barbara Shultz, R.N., B.S.N., Chris McKenna, CRNP, M.S.N., Barbara A. Gaines, M.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.
- 14 ISOLATED CT DIAGNOSIS OF PULMONARY CONTUSION DOES NOT AFFECT MORBIDITY IN PEDIATRIC TRAUMA PATIENTS (3 MINUTES) Albert Kwon, <u>Donald L. Sorrells, Jr., M.D.</u>, John Cassese, M.D., Arlet G. Kurkchubasche, M.D., Thomas F. Tracy, Jr., M.D., Francois I. Luks, M.D., Ph.D., Brown Medical School, Providence, RI, U.S.A.
- 15 FACTORS INFLUENCING PEDIATRIC INJURY SEVERITY SCORE (ISS) AND GLASGOW COMA SCALE (GCS) IN PEDIATRIC AUTOMOBILE CRASHES: RESULTS FROM THE CRASH INJURY RESEARCH ENGINEERING NETWORK (CIREN) (3 MINUTES) Peter F. Ehrlich, M.D.¹, Joanna Brown, M.D.¹, Mark Sochor, ¹, Stewart Wang, ¹, Martin R. Eichelberger, M.D.², ¹University of Michigan, Ann Arbor, MI, U.S.A., ²Children's National Medical Center, Washington, DC, U.S.A.
- 16 DECOMPRESSIVE CRANIECTOMY IN PEDIATRIC TBI PATIENTS WITH REFRACTORY ELEVATED ICP (3 MINUTES) <u>Daniel N. Rutigliano, D.O.¹, Michael R. Egnor, M.D.², Jane E. McCormack, R.N.¹, Nancy A. Strong, R.N., CPNP², Richard J. Scriven, M.D.¹, Thomas K. Lee, M.D.¹, 1Department of Surgery, SUNY Stony Brook, Stony Brook, NY, U.S.A., ²Department of Neurosurgery, SUNY Stony Brook, Stony Brook, NY, U.S.A.</u>
- 17 THE IMPACT OF OBESITY ON SEVERELY INJURED CHILDREN AND ADOLESCENTS (3 MINUTES) <u>Carlos V.R. Brown, M.D.</u>, Angela L. Neville, M.D., Ali Salim, M.D., Peter Rhee, M.D., MPH, Demetrios Demetriades, M.D., Ph.D., LAC/USC Medical Center, Los Angeles, CA, U.S.A.

18 OUTCOMES OF CHILDREN REQUIRING CPR FOLLOWING TRAUMATIC INJURY (3 MINUTES)

<u>Kshama R. Jaiswal, M.D.</u>, Joceyln Chapman, B.S., R. Todd Maxson, M.D., Children's Medical Center Dallas and University of Texas Southwestern Medical Center, Dallas, TX, U.S.A.

- 19 COMPARING TREATMENT OF PEDIATRIC SPLEEN INJURY AT TRAUMA CENTERS VERSUS NON-TRAUMA CENTERS: A CALL FOR DISSEMINATION OF APSA GUIDELINES (3 MINUTES) <u>Steven Stylianos, M.D.</u>¹, Natalia Egorova, Ph.D., MPH¹, Karen S. Guice, M.D.², Ray Arons, DrPH¹, Keith T. Oldham, M.D.³, ¹Children's Hospital of New York, New York, NY, U.S.A., ²APSA Ctr for Outcomes, Milwaukee, WI, U.S.A., ³Children's Hospital of Wisconsin, Milwaukee, WI, U.S.A.
- 20 OUTCOMES AND DELIVERY OF CARE IN PEDIATRIC TRAUMA (3 MINUTES) John C. Densmore, M.D., Keith T. Oldham, M.D., Karen S. Guice, M.D., Children's Hospital of Wisconsin, Milwaukee, WI, U.S.A.
- 21 EFFECT OF CORTICOSTEROID THERAPY ON OUTCOMES IN BILIARY ATRESIA AFTER KASAI PORTOENTEROSTOMY (3 MINUTES) <u>Mauricio A. Escobar, M.D.</u>, Colleen L. Jay, Ronald M. Brooks, Karen W. West, M.D., Frederick J. Rescorla, M.D., Jean P. Molleston, M.D., Jay L. Grosfeld, M.D., Indiana University, Indianapolis, IN, U.S.A.
- 22 RELIEF OF INTRACTABLE PRURITIS IN ALAGILLE SYNDROME BY PARTIAL EXTERNAL BILIARY DIVERSION (3 MINUTES) <u>Peter Mattei, M.D.¹, Daniel von Alllmen, M.D.², David Piccoli, M.D.¹, Elizabeth Rand, M.D.¹, ¹CHOP, Philadelphia, PA, U.S.A., ²UNC, Chapel Hill, NC, U.S.A.</u>
- 23 EFFECTIVENESS OF REX SHUNT IN THE TREATMENT OF PORTAL HYPERTENSION (3 MINUTES)

<u>Roshini Dasgupta, M.D.</u>¹, Eve Roberts, M.D.¹, Riccardo A. Superina, M.D.², Peter C. Kim¹, ¹Hospital for Sick Children, Toronto, ON, Canada, ²Children's Memorial Hospital, Chicago, IL, U.S.A.

Noon – 1 p.m.	International Guest Lecture Prof. Frans W.J. Hazebroek, M.D., Ph.D. "Is Continuation of Life Support Always the Best Option for the Surgical Neonate	Grand Sonoran E/F ?"
1:30 – 3 p.m.	Benji Brooks Meeting and Luncheon	Desert Conference Suite I
2 p.m.	Golf Tournament	Wildfire Golf Club
2 p.m.	Tennis Tournament	Tennis Center
3:15 – 9:30 p.m.	Cattle Drive Activity	Ballroom Entrance
6 – 11 p.m.	Optional Dining Shuttle	Ballroom Entrance
6:30 – 8 p.m.	New Member Reception (invitation only)	Presidential Suite

Tuesday, May 31

6:30 – 8 a.m.	Member business meeting and breakfast	Grand Sonoran G		
6:30 a.m. – 1 p.m.	Registration open	East Registration Desk		
7 a.m. – 2 p.m.	Exhbitis and posters open for viewing	Grand Sonoran A/B, C/D Foyer		
7 – 8 a.m.	Continental breakfast (nonmembers)	Grand Sonoran Foyer		
8 a.m. – Noon	Sonoran Desert Hummer Tour	Ballroom Entrance		
8 – 10 a.m.	Scientific Session III: Gastrointestinal Tract	Grand Sonoran E/F		

Moderators:

- Wallace W. Neblett, III, M.D.
- Daniel H. Teitelbaum, M.D.

Educational Objectives:

Participants attending this session will be provided with current information regarding surgical techniques and long-term outcomes of conditions affecting the gastrointestinal tract in children. Novel basic investigational studies in the pathogenesis of common conditions will also be presented.

24 THE BIANCHI PROCEDURE: A 20-YEAR SINGLE INSTITUTION EXPERIENCE (6 MINUTES) <u>Sonya R. Walker, M.D.</u>, Anita Nucci, Ph.D., R.D., Jane Anne Yaworski, M.S.N., R.N., Edward M. Barksdale, Jr., M.D., FAAP, FACS, Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

- 25 THE ROLE OF LAPAROTOMY FOR INTESTINAL PERFORATION IN VERY LOW BIRTH WEIGHT INFANTS (6 MINUTES) <u>Robert J.V. Baird, MDCM</u>¹, Sebastien Dube, M.Sc.¹, Dickens St.-Vil, MDCM², Jean-Martin Laberge, MDCM, FRCS(c)¹, Pramod S. Puligandla, M.D., M.Sc., FRCS(c)¹, ¹Montreal Children's Hospital, McGill University Health Centre, Montreal, PQ, Canada, ²Hopital Ste. Justine, Montreal, PQ, Canada.
- 26 LAPAROSOPIC NISSEN FUNDOPLICATION WITHOUT DIVISION OF SHORT GASTRIC VESSELS IN CHILDREN: IS "MORE FLOPPY" OVERRATED? (3 MINUTES) <u>Marco V. Melis, M.D.</u>, Mindy B. Statter, M.D., Loretto Glynn, M.D., Tony Lin, M.D., Donald C. Liu, M.D., Ph.D., University of Chicago, Chicago, IL, U.S.A.
- 27 NEW CLINICAL AND THERAPEUTIC PERSPECTIVES IN CURRARINO SYNDROME (STUDIES OF 28 CASES) (6 MINUTES) <u>Claire Nihoul Fékété</u>, Celia Crétolle, Stanislas Lyonnet, Francis Jaubert, Sabine Sarnacki, Hopital des Enfants Malades, Paris, France.
- 28 THE ROLE OF PROLIFERATION AND APOPTOSIS IN THE PATHOGENESIS OF INTESTINAL ATRESIA (6 MINUTES) <u>Timothy J. Fairbanks, M.D.</u>, Frederic Sala, Pierre Del Moral, Jennifer Louise Curtis, M.D., Saverio Bellusci, Ph.D., Kathryn D. Anderson, M.D., Robert Cartland Burns, M.D.,

Tuesday, May 31 (Continued)

Children's Hospital Los Angeles, Los Angeles, CA, U.S.A.

29 OUTCOMES OF ROUX EN Y GASTRIC BYPASS IN ADOLESCENTS: A MULTICENTER REPORT FROM THE PEDIATRIC BARIATRIC STUDY GROUP* (6 MINUTES) Louise Lawson, Ph.D.¹, Shelley Kirk, Ph.D., R.D.¹, Stephen Daniels, M.D., Ph.D.¹, Carroll M. (Mac) Harmon, M.D., Ph.D.², <u>Mike Chen, M.D.³</u>, Victor Garcia, M.D.¹, Thomas Inge, M.D., Ph.D.¹, ¹Cincinnati Children's Hospital Medical Center, Cincinnati, OH, U.S.A., ²Children's Hospital of Alabama, Birmingham, AL, U.S.A., ³University of Florida, Gainesville, FL, U.S.A.

* Dr. Harmon is a consultant for Stryker Endoscopy.

- 30 ATYPICAL MALROTATION: IS OBSERVATION SAFE? (3 MINUTES) <u>Christine M. Habib, M.D.</u>, Richard J. Jackson, M.D., Evan R. Kokoska, M.D., Samuel D. Smith, M.D., Arkansas Children's Hospital, Little Rock, AR, U.S.A.
- 31 HB-EGF DECREASES THE INCIDENCE OF NECROTIZING ENTEROCOLITS IN NEONATAL RATS (6 MINUTES) <u>Jiexiong Feng, M.D., Ph.D.</u>, Osama N. El-Assal, M.D., Ph.D., Gail E. Besner, M.D., Children's Hospital, Columbus, OH, U.S.A.
- 32 HEPATOCYTE GROWTH FACTOR (HGF) INCREASES GLUCAGON IMMUNOREACTIVITY IN JEJUNAL CELLS DURING INTESTINAL ADAPTATION (3 MINUTES) <u>Shaheen J. Timmapuri, M.D.¹, David M. Otterburn, M.D.¹, Hwyda Arafat, M.D., Ph.D.¹, Marshall Z. Schwartz, M.D.², ¹Thomas Jefferson University, Philadelphia, PA, U.S.A., ²Thomas Jefferson University, St. Christopher's Hospital for Children, Philadelphia, PA, U.S.A.</u>
- 33 USE OF A BAYESIAN NETWORK IMPROVES THE ACCURACY OF PHYSICIANS DIAGNOSING INFANTS WITH SUSPECTED PYLORIC STENOSIS (3 MINUTES) <u>Sonia M. Alvarez, M.D.</u>, Beverly A. Poelstra, M.D., Randall S. Burd, M.D., Ph.D., UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.

10 – 10:30 a.m.	Refreshment break	Grand Sonoran Foyer
10:30 a.m. – Noon	Scientific Session IV: Cancer	Grand Sonoran E/F

Moderators:

- Stephen J. Shochat, M.D.
- Daniel von Allmen, M.D.

Educational Objectives:

The participants in this session will be presented with the latest advances in the treatment of pediatric cancer and provocative insights into cancer biology from pre-clinical investigative work.

Tuesday, May 31 (Continued)

34 VALUE OF SURGERY IN DIRECTING THERAPY OF WILMS TUMOR PATIENTS WITH PULMONARY DISEASE. A REPORT FROM NATIONAL WILMS TUMOR STUDY (NWTS) – 5 (6 MINUTES)

Peter F. Ehrlich, M.D.², <u>Tom E. Hamilton, M.D.¹</u>, Robert C. Shamberger, M.D.³, Michael Ritchey, M.D.⁴, Gerald Haase, M.D.⁵, Paul Grundy⁶, ¹Main Medical Center, Portland, ME, U.S.A., ²University of Michigan, Ann Arbor, MI, U.S.A., ³Harvard University, Boston, MA, U.S.A., ⁴University of Texas, Houston, TX, U.S.A., ⁵Denver Children's Hospital, Denver, CO, U.S.A., ⁶Alberta Children's Hospital, Edmonton, AB, Canada.

- 35 PRIMARY HEPATIC METASTASES IN NEPHROBLASTOMA A REPORT OF THE SIOP/GPOH STUDY (6 MINUTES) <u>Philipp O. Szavay, M.D.¹, Norbert Graf, M.D., Ph.D.², Tobias Luithle, M.D.¹, Rhoikos Furtwängler², Joerg Fuchs, M.D., Ph.D.¹, ¹University of Tuebingen, Tuebingen, Germany, ²University of Homburg/Saar, Homburg, Germany.</u>
- 36 TUMOR INHIBITION CORRESPONDS TO PERTURBATION AND RECOVERY OF VASCULATURE DURING SUSTAINED POTENT VEGF BLOCKADE (3 MINUTES) <u>Angela V. Kadenhe-Chiweshe, M.D.</u>, Jason Frischer, M.D., Jae-O Bae, M.D., Jianzhong Huang, M.D., Jessica Kandel, M.D., Darrell Yamashiro, M.D., Columbia University, New York, NY, U.S.A.
- 37 STUDY OF THE FACTORS ASSOCIATED WITH RECURRENCE IN CHILDREN WITH SACROCOCCYGEAL TERATOMA (3 MINUTES) <u>Toon De Backer, M.D.</u>, Gerard Madern, M.D., Friederike Hakvoort, M.D., Frans W.J. Hazebroek, M.D., Ph.D., Academic Hospital, Free University of Brussels, Brussels, Belgium and Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands.
- 38 LIVER TRANSPLANTATION FOR CHILDHOOD HEPATIC MALIGNANCY: IS IT A VIABLE OPTION? (3 MINUTES) <u>Mary T. Austin, M.D.</u>, Charles M. Leys, M.D., Irene D. Feurer, M.D., Harold N. Lovvorn, M.D., James A. O'Neill, M.D., C. Wright Pinson, M.D., M.B.A., John B. Pietsch, M.D., Vanderbilt University Medical Center, Nashville, TN, U.S.A.
- 39 SURVIVAL AFTER LIVER TRANPLANTATION FOR HEPATOBLASTOMA: A TWO CENTER EXPERIENCE (3 MINUTES) <u>Marybeth Browne, M.D.¹, Dani Sher, B.A.¹, Lisa P. Abramson, M.D.¹, David Grant, M.D.², Enza Deluca, R.N.², Estella Alonso, M.D.¹, Peter F. Whitington, M.D.¹, Riccardo A. Superina, M.D.¹, ¹Children's Memorial Hospital, Chicago, IL, U.S.A., ²Hospital for Sick Children, Toronto, ON, Canada.</u>
- 40 CLINICAL PRESENTATION, TREATMENT, AND OUTCOME OF ALVEOLAR SOFT PART SARCOMA IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS (3 MINUTES) Mark L. Kayton, M.D., Paul Meyers, M.D., Leonard H. Wexler, M.D., <u>Michael P.</u> <u>LaQuaglia, M.D.</u>, Memorial Sloan-Kettering Cancer Center, New York, NY, U.S.A.

Tuesday, May 31 (Continued)

- 41 OPEN THORACOTOMY IS THE BEST THERAPY FOR METASTATIC OSTEOGENIC SARCOMA (3 MINUTES) <u>Mark L. Kayton, M.D.</u>, Jennifer Casher, B.A., Sara J. Abramson, M.D., Nancy S. Rosen, M.D., Leonard H. Wexler, M.D., Paul Meyers, M.D., Michael P. LaQuaglia, M.D., Memorial Sloan-Kettering Cancer Center, New York, NY, U.S.A.
- 42 LONG-TERM SURVIVAL AFTER AGGRESSIVE RESECTION OF PULMONARY METASTASES AMONG PATIENTS WITH OSTEOSARCOMA (3 MINUTES) <u>Matthew T. Harting, M.D.¹, Martin L. Blakely, M.D.², Norman Jaffe, M.D., D.Sc.³, Charles S. Cox, Jr, M.D.¹, Andrea Hayes-Jordan, M.D.¹, Robert S. Benjamin, M.D.³, Richard J. Andrassy, M.D.¹, Kevin P. Lally, M.D.¹, ¹University of Texas Medical School at Houston, Houston, TX, U.S.A., ²University of Tennessee Health Science Center, Memphis, TN, U.S.A., ³MD Anderson Cancer Center, Houston, TX, U.S.A.</u>
- 43 C-MYC INHIBITION NEGATIVELY IMPACTS LYMPHOMA GROWTH (6 MINUTES) <u>R. Serene Perkins, M.D.</u>, Stephen P. Dunn, M.D., Ilsa Gomez-Curet, Ph.D., Katherine L. Feidler, B.S., Leslie J. Krueger, Ph.D, AI duPont Hospital for Children, Wilmington, DE, U.S.A.

Noon – 1:15 p.m.	Welcome New Members/ Presidential Address Robert J. Touloukian, M.D. "The Ultimate Commencement"	Grand Sonoran E/F
1:15 – 1:30 p.m.	Refreshment break	Grand Sonoran Foyer
1:30 – 3:30 p.m.	Telesurgery demonstration with lunch	Grand Sonoran E/F
2 p.m.	Exhibits dismantle	Grand Sonoran Foyer
3:45 – 5:15 p.m.	COG Surgeons' Meeting (open to all APSA meeting attendees)	Grand Sonoran E/F
6:30 – 7:15 p.m.	President's Reception	Grand Sonoran Foyer
7:15 – 10:30 p.m.	President's Banquet	Grand Sonoran E/F

Wednesday, June 1

7 – 11:15 a.m.	Posters open for viewing	Grand Sonoran A/B Grand Sonoran C/D
7 – 8 a.m.	Continental breakfast	Grand Sonoran Foyer
7:30 – 11:30 a.m.	Registration open	East Registration Desk
8 – 8:15 a.m.	APSA Foundation Scholar Karl Sylvester, M.D. "Liver Regeneration and Stem Cell Regulation via the WNT Signaling Pathway"	Grand Sonoran E/F

Wednesday, June 1 (Continued)

8:15 – 8:30 a.m.	APSA Foundation Scholar Christopher K. Breuer, M.D. "Do Tissue Engineered Venous Conduits Grow? Investigating the Growth Potential of Tissue Engineered Venous Conduits in a Juvenile Lamb Model"	Grand Sonoran E/F
8:30 – 9:30 a.m.	Journal of Pediatric Surgery Lecture Alberto Peña, M.D. "Luck and Serendipity, the History of a Surgical Technique"	Grand Sonoran E/F
9:30 – 11:15 a.m.	Scientific Session V: Congenital Anomalies and Neonatal Critical Care	Grand Sonoran E/F

Moderators:

- Edward M. Barksdale, Jr., M.D.
- Daniel H. Teitelbaum, M.D.

Educational Objectives:

Presentations in this session will provide the attendee with information regarding emerging techniques for the surgical management of challenging congenital anomalies in pediatric surgery. This session will also provide the participant with critical care evolving concepts in the critical care of surgical neonates.

44 THE LAPAROSCOPIC APPROACH TO THE MANAGEMENT OF CONGENITAL HYPERINSULINISM OF INFANCY (6 MINUTES) <u>Agostino Pierro, M.D.¹, Virpi Smith, Ph.D.¹, Keith Lindley, M.D.², Peter Hindmarsh, M.D.², Mehul Dattani, M.D.², Khalid Hussain, M.D.¹, ¹Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom, ²Great Ormond Street Hospital for Children, London, United Kingdom.</u>

 45 VACUUM ASSISTED CLOSURE (V.A.C.): A NEW METHOD FOR TREATING PATIENTS WITH OMPHALOCELE (3 MINUTES) <u>Kandice E. Kilbride, M.D.</u>, Donald R. Cooney, M.D., Monford D. Custer, M.D., Texas A & M – Scott and White, Temple, TX, U.S.A.

 46 THE USE OF HUMAN ACELLULAR DERMIS IN THE OPERATIVE MANAGEMENT OF GIANT OMPHALOCELE* (3 MINUTES) <u>Stephanie A. Kapfer, M.D.</u>, Tamir H. Keshen, M.D., Washington University School of Medicine, St. Louis Children's Hospital, St. Louis, MO, U.S.A.
* Author received a travel grant from LifeCell Corp.

47 PROGNOSTIC FACTORS IN SURGICAL TREATMENT OF CONGENITAL TRACHEAL STENOSIS (CTS) AND A MULTI-CENTER ANALYSIS OF THE LITERATURE (3 MINUTES) <u>Priscilla P. Chiu, M.D., Ph.D.,</u> Derek Stephens, M.Sc., Vito Forte, Peter C. W. Kim, M.D., Ph.D., The Hospital for Sick Children, Toronto, ON, Canada.

Wednesday, June 1 (Continued)

- 48 RISK FACTORS FOR MAJOR VENOUS THROMBOEMBOLIC EVENTS AMONG CHILDREN UNDERGOING ABDOMINAL SURGERY (3 MINUTES) <u>Randall S. Burd, M.D., Ph.D.</u>, Marissa D. Newman, B.S., Stacey B. Trooskin, MPH, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.
- 49 AORTOILLIAC RECONSTRUCTION USING BRANCHED PULMONARY ARTERY ALLOGRAFT (3 MINUTES) <u>Rebecka L. Meyers, M.D.</u>, John A. Hawkins, Larry W. Kraiss, University of Utah, Salt Lake City, UT, U.S.A.
- 50 SEVERE PULMONARY HYPOPLASIA ASSOCIATED WITH GIANT CERVICAL TERATOMAS (3 MINUTES) <u>Kenneth W. Liechty</u>, Holly L. Hedrick, M.D., Mark P. Johnson, M.D., R. Douglas Wilson, M.D., Eduardo D. Ruchelli, M.D., Lori J. Howell, R.N., M.S., Timothy M. Crombleholme, M.D., Alan W. Flake, M.D., N. Scott Adzick, M.D., The Children's Hospital of Philadelphia, Philadelphia, PA, U.S.A.
- 51 RELATIVE VALUE UNITS CORRELATE WITH PEDIATRIC SURGEONS' OPERATING TIME: WHEN PERCEIVED MYTH BECOMES REALITY (3 MINUTES) <u>Danny C. Little, M.D.</u>, Shawn D. St. Peter, M.D., Casey M. Calkins, M.D., George K. Gittes, M.D., Daniel J. Ostlie, M.D., Charles L. Snyder, M.D., Children's Mercy Hospital, Kansas City, MO, U.S.A.
- 52 TPN-ASSOCIATED HYPERGLYCEMIA CORRELATES WITH PROLONGED MECHANICAL VENTILATION AND HOSPITAL STAY IN SEPTIC PREMATURE INFANTS (3 MINUTES) <u>Diya I. Alaedeen, M.D.</u>, Michele C. Walsh, M.D., Walter J. Chwals, M.D., University Hospitals of Cleveland, Rainbow Babies and Children's Hospital, Cleveland, OH, U.S.A.
- 53 THE EFFECTS OF INSULIN ON PROTEIN METABOLISM IN CRITICALLY ILL NEONATES (3 MINUTES) <u>Hannah G. Piper, M.D.¹, Patrick J. Javid, M.D.¹, Michael S. Agus, M.D.¹, Daniel P. Ryan, M.D.², Tom Jaksic, M.D., Ph.D.¹, ¹Children's Hospital Boston, Boston, MA, U.S.A., ²Massachussetts General Hospital, Boston, MA, U.S.A.</u>

11:15 a.m.	Annual meeting adjourns/posters dismantle	
Noon – 3 p.m.	Executive Council for Pediatric Surgery Organizations	Grand Sonoran H

ABSTRACTS

Video Session

V1 USE OF THE STRETTA PROCEDURE FOR RADIOFREQUENCY ABLATION OF THE LOWER ESOPHAGEAL SPHINCHTER IN CHILDREN WITH GASTROESOPHAGEAL REFLUX DISEASE*

<u>Ariel U. Spencer, M.D.</u>¹, Donald C. Liu, M.D., Ph.D.², Daniel H. Teitelbaum, M.D.¹, ¹University of Michigan, Ann Arbor, MI, U.S.A., ²University of Chicago, Chicago, IL, U.S.A. *Author will discuss the Stretta procedure as an investigational use in pediatric patients.

PURPOSE:

Children with gastroesophageal reflux disease (GERD) who fail pharmacologic and medical management often require a fundoplication. Increasingly, endoscopic modalities to treat GERD have been utlized in adults. This video describes the use of radiofrequency ablation of the lower esophageal sphinchter (Stretta procedure) as another means of treating this disorder in pediatric patients.

METHODS:

The video details the indications, workup and technique of this proceudre. In particular, it discusses variations of this technique which pertain to the pediatric patient, and in those children who have this procedure performed after a fundoplication.

RESULTS:

Results overall have been excellent for the procedure and well tolerated.

CONCLUSIONS:

The Stretta procedure should be considered for pediatric patients with recurrent reflux, and possibly primary reflux disease.

V2 MODIFIED NUSS PROCEDURE: TECHNIQUES FOR ASYMMETRIC PECTUS EXCAVATUM <u>Hyung Joo Park, M.D.</u>, Seung Jin Lee, M.D., Seock Yeol Lee, M.D., Cheol Sae Lee, M.D., Soonchunhyang University Chunan Hospital, Chunan, Republic of Korea

PURPOSE:

In dealing with asymmetric morphological varieties of pectus excavatum (PE), the conventional Nuss technique, correcting a single target with a symmetric bar, has not been successful to achieve a post-repair symmetry. To solve this problem, we have developed several new techniques under the concept of multi-target approach for the repair of asymmetric PE. We present our modified techniques, which are individually designed for each specific type of asymmetry.

METHODS:

Two patients with different types of asymmetric PE were repaired with our modified techniques. The first patient was 13-year-old male who had an Eccentric Long Canal type PE (Type 2A3, Grand Canyon type). Repair techniques are Asymmetric Bar, Parallel Bar, and Multipoint Fixation (End-Hole Fixation + Hinge Point Fixation) techniques. The second patient was a 6-year-old boy who had an Unbalance type PE (Type 2B). Asymmetric Seagull Bar, Crest Compression, and Multipoint Fixation techniques were applied. Results of the repair are assessed by means of new Computerized Tomogram (CT) indices: particularly the Depression Index (DI) and Asymmetry Index (AI).

RESULTS:

For eccentric type (patient 1), asymmetric bar technique is effective in elevating precisely the selective portion of eccentric depression to the level without affecting the other side. For unbalanced asymmetry (patient 2), a protrusion-depression complex, crest compression technique can resolve the multiple target by compressing the protruding crest and elevating the depressed area simultaneously (Figure 1). Pre and postoperative CT Indices are DI: 2.56; 2.04 vs. 1; 1 and AI: 1.16; 1.22 vs. 1.02; 1.03, respectively.

CONCLUSIONS:

Our modified techniques tailored to each specific type of asymmetry seem to be effective in repair of asymmetric PE. Postoperative changes of AI suggest that the post-repair symmetry is achieved in both cases.



Figure 1. Unbalanced type with chest wall protrusion (*): Repair with Crest Compression Technique (Double Target Approach): simultaneous elevation and compression of targets by making the protruded crest a hinge point (inset: seagull bar and mechanism of double action).

* Crest = Hinge: protruded crest is compressed upon bar rotation which accomplishes post-repair symmetry a = axis of bar: declined along the hinge plane; H, H' = hinge points; H-H' = hinge plane Preop. = preoperative CT scan; Postop. = postoperative CT scan.

V3 VIDEO-ASSISTED THORACOSCOPIC SURGICAL EXCISION OF A RIGHT UPPER LOBE CPAM <u>Curt S. Koontz, M.D.</u>, Kenneth Gow, M.D., Mark L. Wulkan, M.D., Emory University School of Medicine, Atlanta, GA, U.S.A.

This video is a right upper lobe pneumonectomy performed in a 4-month-old twin female with a right sided chest mass. The patient was born at 33 weeks gestation weighing 1630 grams. Prenatally, a right sided chest mass was detected on ultrasound. At birth, her respiratory status was stable with a room air saturation of 99%. A chest CT suggested a right lower lobe congenital pulmonary airway malformation (CPAM). At the age of four months, she weighed 4.8 kg and was felt to be in good condition for an elective thoracoscopic lobectomy. She subsequently underwent a video-assisted thoracoscopic exploration. Upon exploration the lesion was found to be in her right upper lobe, and a right upper lobectomy was performed. Pathology confirmed a CPAM. Her postoperative course was unremarkable. The chest tube was removed on post-operative day one and she was discharged home on post-operative day two. At post-operative follow-up, she is doing well.

V4 MINIMALLY INVASIVE THORACOSCOPIC ULTRASOUND (MITUS) FOR RESECTION OF PULMONARY NODULES <u>Kenneth W. Gow, M.D.</u>, Mark L. Wulkan, M.D., Emory University, Atlanta, GA, U.S.A.

BACKGROUND:

Thoracotomy is considered the standard approach for resection of pulmonary nodules. Recently, thoracoscopic techniques have been used for these lesions. However, nodules that are deep in the lung parenchyma may not be visible or palpable. We have developed a technique whereby minimally invasive thoracoscopic ultrasound (MITUS) may be used to guide resection of pulmonary nodules.

METHODS:

The patient is intubated with a double lumen endotracheal tube and positioned in a decubitus manner with the ipsilateral lung up. Two 5 mm ports are inserted, one for the grasper and the other for the camera. One 12 mm port is inserted for the flexible 10 mm ultrasound probe and the endoscopic stapler. The patient has CO² insufflation to create a 5-mmHg pneumothorax. 20 cc/kg of normal saline is introduced into the pleural cavity for acoustic coupling. The ultrasound probe is used to isolate the nodule(s), guide resection, and check margins. The specimen is removed in an endoscopic bag to limit port site metastases. After the lung has been inspected, irrigation is removed, and a chest tube inserted.

RESULTS:

MITUS has been applied in three patients; a 13-year-old male with metastatic osteosarcoma in the right lower lobe, a 13-year-old male with ALL with an abscess in the left lower lobe, and a 17-year-old male with osteosarcoma who was noted to have a nodule in the right lower lobe on CT scan which was found to be a lymph node on histology. All patients had an adequate specimen for diagnosis and had margins clear of disease. There were no complications and no conversions to thoracotomy.

CONCLUSION:

MITUS is a real-time imaging tool that helps guide resection of pulmonary lesions that otherwise might require thoracotomy. It may also allow the remaining lung parenchyma to be inspected for occult lesions.

V5 ROBOTIC EXCISION OF CHOLDOCHAL CYST <u>James D. Geiger, M.D.</u>, Oliver S. Soldes, M.D., University of Michigan, Ann Arbor, MI, U.S.A.

PURPOSE:

Choledochal cyst can present at any age with abdominal pain, jaundice, cholangitis, and pancreatitis being frequent presenting symptoms. Early diagnosis followed by cyst excision and Roux-en-Y reconstruction of the biliary tract is the treatment of choice, even in asymptomatic children. Because of the complexity of this operation, minimally invasive approaches have not been widely used. We explore the use of robotics to facilitate a lapaproscopic approach.

METHODS:

A 4-year-old girl presented with abdominal pain initially thought to be appendicitis. When she didn't improve after an appendectomy she was found to have pancreatitis and a rightupper quadrant cystic mass by ultrasound. Magnetic resonance cholangiopancreatography (MRCP) was obtained which confirmed the diagonosis of a Type I choledochal cyst. After the patient's pancreatits resolved she underwent elective excision of the cyst. A total of 5 ports were used in a somewhat similar configuration as utilized for laparaoscopic chlolecystectomy. The fundus of the gallbladder was left intact to provide upward traction. The da Vinci robot was utilized for the complete dissection and excision of the cyst as well as the Roux-en-Y hepaticojejunostomy. A stapled jejunostomy was completed laparoscopically to complete the procedure.

RESULTS:

The operative time was 432 minutes and there were no intra-operative complications. The patient was discharged home on the sixth postoperative day tolerating regular diet. She had an afferent limb obstruction four weeks postoperatively, but is currently doing well with normal liver function and no bouts of cholangitis.

CONCLUSIONS:

This early experience indicates that robotic excision of choledochal cyst and Roux-en-Y reconstruction is feasible and may allow this procedure to be completed more commonly with a minimally invasive approach.

 V6 LAPAROSCOPIC HEPATOPORTO-ENTEROSTOMY (KASAI PROCEDURE) <u>Hanmin Lee, M.D.</u>¹, Matthew S. Clifton, M.D.², Michael Harrison, M.D.³, Kerilyn Nobuhar, M.D.³, Erich Grethel, M.D.³, Raul Cortes, M.D.³, Diana Farmer, M.D.³, ¹University of California (Division of Pediatrics), San Francisco, CA, U.S.A., ²University of California (Divison of Pediatric Surgery), San Francisco, CA, U.S.A., ³University of California (Division of Pediatric Surgery), San Francisco, CA, U.S.A.

PURPOSE:

To determine the feasibility of performing a hepatoportoenterostomy (Kasai Procedure) via laparoscopic techniques.

METHODS:

All image and data collection, analysis, and presentation of this study were done under IRB approval. A zero-degree, 2.7 mm laparoscope was inserted via an umbilical 3.0 mm radially dilating trocar. Three additional 3.0 mm or 5.0 mm radially dialating trocars were inserted below the costal margin. The porta hepatis was exposed using the gallbladder and falciform ligament for retraction. The distal anastamosis of the Roux-en-Y was performed extracorporally. The remainder of the operation, including portoenterostomy, was performed laparoscopically.

RESULTS:

Approximate operating time was six hours. Excellent exposure can be achieved using the gallbladder remnant (as in a cholecystectomy) to retract the liver and expose the porta hepatis.

CONCLUSIONS:

Laparoscopic hepatoportoenterostomy is a feasible operation and should be considered as an alternative to the traditional open method.

Poster Session IA: Hematology and Oncology

P1 STRUCTURAL ANALYSIS OF THE HUMAN NEUROBLASTOMA DNA REPLICATION COMPLEX: INSIGHTS INTO FAULTY PROLIFERATION John A. Sandoval, M.D., Jay L. Grosfeld, M.D., Robert J. Hickey, Ph.D., Linda H. Malkas, Ph.D., Indiana University School of Medicine, Indianapolis, IN, U.S.A.

PURPOSE:

Neuroblastoma (NB) DNA replication and whether faulty DNA synthesis contributes to malignancy has received little attention. We have previously shown that DNA replication in NB is orchestrated by a multiprotein DNA replication complex (DNA synthesome). It has been demonstrated that the DNA synthesome in NB mediates an error prone DNA replication process. The aim of this study is to define structural alterations of the NB DNA synthesome proteins which lead to lowered replication fidelity.

METHODS:

Three dimensional NB (SK-N-AS, SK-N-DZ, and IMR-32) and neural stem (M009 and M027) cell culture models were utilized to purify the DNA synthesome. Proteomic differences associated with the DNA synthesome in NB versus nonmalignant neural stem (NS) cells were determined using two dimensional polyacrylamide electrophoresis (2-D PAGE) and Western blotting.

RESULTS:

Proteins of the DNA synthesome [DNA polymerases α , δ , and ε , Proliferating cell nuclear antigen (PCNA), Replication protein-A (RPA), Flap endonuclease-1 (FEN-1), DNA ligase I, topoisomerases I and II) from human NB and NS cells were compared. Among the proteins analyzed, only RPA showed multiple isoforms in NB that were distinct from nonmalignant NS cells. The 34 kDa subunit of the heterotrimer RPA from NS cells was resolved as a single spot with a pl value of 5.75. However, NB cell RPA showed a main spot (pl 5.75), as well as two acidic and one basic isoforms. RPA binds to single-stranded DNA and participates in multiple protein-protein interactions.

CONCLUSIONS:

The NB DNA synthesome showed three distinct isoforms of RPA when compared to NS cells. These findings are significant in that it is now possible to link changes in the fidelity of DNA replication with a specific alteration of a component of the DNA synthetic apparatus of NB. The novel forms of RPA may prove to be a new signature of malignancy in NB.

P2 MIS INHIBITS TUMOR GROWTH IN VIVO IN A NEW ANIMAL MODEL, WHICH RECAPITULATES HUMAN OVARIAN CANCER <u>Rafael Pieretti-Vanmarcke, M.D.¹, David T. MacLaughlin, Ph.D.¹, Denise Connolly, Ph.D.², Patricia K. Donahoe, M.D.¹, ¹Massachusetts General Hospital, Boston, MA, U.S.A.,</u>

²Fox Chase Cancer Center, Philadelphia, PA, U.S.A.

PURPOSE:

Ovarian cancer is the third most common gynecological cancer, with 25,000 new patients per year and aproximately14,000 cancer related deaths per year. Mullerian Inhibiting Substance (MIS), a biological modifier developed in this laboratory, causes regression of the Mullerian duct in male embryos. We propose that MIS is an effective anticancer drug *in vivo* against tumors that express MIS type II receptor and can be used cooperatively with cytotoxic agents in clinical use.

METHODS:

Mouse ovarian carcinoma cell lines (MOVCAR) expressing MISIR-directed T antigen developed in transgenic mice by Denise Connolly, Ph.D., Fox Chase Cancer Center, were tested *in vivo* after xenotransplantation in Swiss, female nude mice, six weeks old, against MIS alone, and *in vitro* against MIS alone and in combination with Doxorubicin, Paclitaxel and Cisplatin. Tissue and cells were analyzed by Northern, immunohistochemestry, and growth inhibition assays.

RESULTS:

MOVCAR cells express MISIIR by Northern (n=2 experiments). MIS inhibited MOVCAR cell growth *in vitro* by 70 - 95% compared with vehicle controls (n=8, p< 0.05). MIS also inhibited MOVCAR cell growth *in vivo* (n=3, p<0.05) in xenotransplanted mice. MIS, drug, and the combination when compared to control treatment showed a statistically significant difference by t test (n=10, p< 0.05). By Two-way Factorial Analysis of Variance we tested whether the effect of the combination therapy was different from what one would predict by using each drug alone. With the interaction term (MIS x Doxorubicin) (n=2, p=0.023), the pair was synergistic; with (MIS x Paclitaxel) (n=4, p=0.413) the pair appeared to be additive; Cisplatin and MIS appeared to be neither synergistic nor additive.

CONCLUSIONS:

MIS is an effective anticancer drug *in vivo* and *in vitro* against tumors that express MISRII and can be used cooperatively with cytotoxic agents presently in clinical use.



Figure 1: Volume +/- SEM of MOVCAR tumors in the dorsal fat pad of nude mice (n=5 per group), with and without MIS treatment. *Significant from control, p < 0.05.

Underlining denotes the author scheduled to present at the meeting.

Final Program

P3 REGULATORY EFFECT OF NERVE GROWTH FACTOR ON THE ERK1 PATHWAY IN WILD-TYPE, DOXORUBICIN-RESISTANT, AND NERVE GROWTH FACTOR-TRANSFECTED NEUROBLASTOMA CELL LINES <u>Bill Chiu, M.D.</u>, Bernard Mirkin, Ph.D., M.D., Robert Arensman, M.D., Mary Beth Madonna, M.D., Children's Memorial Hospital, Northwestern University Feinberg School of Medicine, Chicago, IL, U.S.A.

PURPOSE:

Neuroblastoma cells that expresses TrkA, a nerve growth factor (NGF) receptor, have been associated with a more favorable prognosis. We evaluated the effect of NGF on the ERK1 pathway in three neuroblastoma cell lines with differing characteristics.

METHODS:

Doxorubicin-resistant cells were generated by incubating wild-type SK-N-SH cells in incremental concentrations of doxorubicin. NGF-transfected cells were engineered by transfecting wild-type cells with a retroviral vector containing the NGF gene. Cells were synchronized at G0-phase by incubation in serum-free medium and incubated for five-minute, one and 16 hours with NGF (100ng/ml). Whole cell lysates were then prepared. Western immunoblots were performed with antibodies against Ras, Raf, MEK1/2, and Erk1. Optical density of the developed bands was measured, and activation determined by the ratio of phosphorylated form to total. The percentage change in ratio of optical density between experimental and control cells was used to quantify response. Data from three independent experiments were averaged for statistical analysis.

RESULTS:

Ras expression and Raf activation did not change appreciably in any cell lines after NGF incubation. For wild-type cells, NGF increased MEK1/2 activation 58% above control after a five-minute incubation and ERK1 28% after one hour. For the doxorubicin-resistant cells, NGF incubation decreased activation of MEK1/2 27% and ERK1 61% after one hour. For NGF-transfected cells, NGF incubation increased activation of MEK1/2 22% and ERK1 68% after 16 hours.

CONCLUSIONS:

Incubation of wild-type and NGF-transfected cells with NGF increased activation of MEK1/2 and ERK1. Exogenous NGF caused additional activation despite constitutive production of NGF in NGF-transfected cells, suggesting availability of more receptors for NGF binding. In contrast, NGF decreased the activation of MEK1/2 and ERK1 in doxorubicin-resistant cells. Since the activation of ERK1 is associated with cell survival, we hypothesize that NGF could serve as a potential treatment for doxorubicin-resistant neuroblastoma cells.

Notes:

P4 DIFFERENTIAL SIGNALING RESPONSE OF NEUROBLASTOMA TO MEK ACTIVITY INHIBITOR TREATMENT PREDICTS RESISTANCE TO MAP KINASE BASED TREATMENT STRATEGIES

<u>Andrew C. Eppstein, M.D.</u>, John A. Sandoval, M.D., Patrick J. Klein, Ph.D., Heather A. Woodruff, B.S., Jay L. Grosfeld, M.D., Robert J. Hickey, Ph.D., Linda H. Malkas, Ph.D., Christian M. Schmidt, M.D., Ph.D., Indiana University School of Medicine, Indianapolis, IN, U.S.A.

PURPOSE:

Neuroblastoma is a heterogeneous tumor comprised of neuroblastic (N), non-neuronal, substrate-adherent (S), and intermediate (I) cells. Since cell growth and differentiation depend upon mitogen-activated protein kinase (MAPK) pathway signaling, we explored the MAPK signaling and growth response in three NB cell types following exposure to MAP kinase kinase (MEK) inhibitor to evaluate the feasibility of targeted treatment strategies.

METHODS:

Three human NB cell cultures, SH-SY5Y (N-type), BE(2)-C (I-type), and SK-N-AS (S-type) were treated with increasing concentrations (0.1 to 10 μ M) of U0126, a potent MEK inhibitor. MAPK pathway intermediates MEK and ERK concentrations, their activated (phosphorylated) forms p-MEK and p-ERK, and p53 expression were assessed by Western blot at one and 24 hours. Cellular growth was determined at 72 hours by proliferation assays and Coulter Counter analysis.

RESULTS:

In all lines, total ERK and MEK remained constant at one and 24 hours at all U0126 concentrations. At one hour MEK activity decreased, demonstrated by inhibition of p-ERK with increasing U0126 concentrations; conversely, p-MEK levels increased with increasing U0126 concentrations. At 24 hours, all lines exhibited continued p-ERK suppression, although N-type cells had recovery of p-ERK towards baseline levels. P-MEK expression increased in all lines at 24 hours. I-type growth decreased with increasing U0126 concentrations while N- and S-types showed significant growth inhibition only at higher U0126 doses. N-type was the least growth-inhibited, corresponding to quickest p-ERK recovery. N-type expressed low p53 activity, which was upregulated in S and I types.

CONCLUSIONS:

Significant differences in MAPK signaling in NB were detected through MEK inhibition. N-type cells resisted MEK inhibition, while S-type and I-type had intermediate and high sensitivity. Low p53 expression in the N-type suggests reduced apoptosis. Different NB cell lines have dissimilar MAPK pathway responses to MEK inhibition, which may predict N-type NB resistance to MAPK-based treatments.

P5 INDUCTION OF IMMUNE RESPONSES TO, AND IDENTIFICATION OF, SHARED TUMOR ASSOCIATED ANTIGENS IN RHABDOMYOSARCOMA <u>David A. Rodeberg, M.D.</u>, Courtney Erskine, B.S., Esteban Celis, M.D., Mayo Foundation, Rochester, MN, U.S.A.

PURPOSE:

Rhabdomyosarcoma (RMS) is the most common sarcoma in childhood. Currently, novel therapies to improve survival of these patients are being investigated. One of the new approaches involves immunotherapy using tumor specific T-lymphocytes. An effective prolonged immune mediated response against tumor cells is dependent upon recognition and response of Helper T-lymphocytes (HTL) to tumor associated antigens (TAA) in the presence of histocompatibility lymphocyte antigen (HLA) surface proteins.

METHODS:

RMS tumor lysate-pulsed dendritic cells (DC) were used to stimulate HTL precursors (naive CD4+ T-cells) in tissue culture. After three rounds of antigen stimulation with antigen presenting cells (APC), the T-cells were tested for reactivity (T-cell proliferation assays) against a large panel of tumor lysate-pulsed autologous APC.

RESULTS:

Using PBMCs from normal naive donors we have been able to generate HTL clones that recognize and proliferate to multiple tumor cell lines. The HTL were induced using lysate from a single ARMS tumor cell line (RMS13). The clones generated recognized all of the ARMS cell lines (RMS 13, Rh 18, Rh28, Rh30, and Rh41), prostate cancer cell lines (LNCAP and LAPC4), melanoma cell lines (Mel 624 and G361), and breast cancer cell line (SKBR3). HTL recognition was also confirmed by interferon-gamma production. The clones did not recognize colon, lymphoma, ERMS or EBV transformed B-cells. This recognition was HLA class II restricted and was not an allogeneic response.

CONCLUSIONS:

The clinical significance of this work cannot be understated since the overall survival for patients with ARMS, especially for those with metastatic disease, is poor. The methods and techniques developed here may be translated to clinical practice resulting in new therapeutic modalities that have minimal toxicities and are tumor specific.



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P6 NEUROBLASTOMA IMPAIRS CHEMOKINE-MEDIATED DENDRITIC CELL MIGRATION IN VITRO Sonya R. Walker, M.D., <u>P. Dafé Ogagan, B.S.</u>, Alex Aboka, B.S., Edward M. Barksdale, Jr., M.D., FAAP, FACS, Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

PURPOSE:

Chemokine receptor (CCR7) and ligand (CCL19) interactions trigger DC recruitment from sites of antigen uptake to secondary lymphoid organs for T cell priming and tumor lysis. Inhibition of this interaction may allow some aggressive tumors to evade immune detection. Although we have shown dysfunctional DC migration in murine neuroblastoma (NB) *in vivo*, the molecular mechanisms of impairment are unknown. We hypothesize that NB-induced aberrant CCR7-CCL19 signaling impairs DC migration.

METHODS:

Bone marrow-derived DC were isolated from A/J mice (n=12), matured and co-cultured with murine NB (TBJ) or media (control) for seven days. CCR7 and CCL19 protein and mRNA expression were measured by Western blot analysis, polymerase chain rection and flow cytometry. Migration assays using Transwell[®] plates were performed with CCL19. Furthermore, to determine if these changes in migration could be overcome, super-physiologic concentrations of CCL19 (5-100 ng/mL) were used to stimulate DC. Results are reported as the average percent ± standard deviation.

RESULTS:

No significant differences in CCR7 or CCL19 protein expression between tumor and control were seen at seven days. However, NB significantly decreased CCL19-induced migration by > 50%: control (26.48 \pm 1.52%) versus DC co-cultured with TBJ (12.7 \pm 0.3%), p<0.05. Super-physiologic doses up to 100 ng/mL CCL19 showed no significant upregulation in migration in DC co-cultured with tumor.

CONCLUSIONS:

Although *in vitro* co-culture with NB does not induce significant changes in either CCR7 or CCL19 expression, profound functional impairments in CCR7/CCL19-mediated migration occurs. These findings suggest that intracellular signal transduction pathways for these chemokines may be impaired by tumor. Targeting this chemokine-receptor pathway may provide a novel therapeutic strategy.



P7 PI3 KINASE MEDIATES BILE SALT INDUCED PROLIFERATION IN A TELOMERASE IMMORTALIZED BARRETT'S CELL LINE <u>Kshama R. Jaiswal, M.D.</u>¹, Christie Lopez-Guzman, B.S.¹, Fiemu Nwariaku, M.D.¹, Thomas Anthony, M.D.¹, R. Todd Maxson, M.D.², George A. Sarosi, M.D.¹, 1University of Texas Southwestern and Dallas VAMC, Dallas, TX, U.S.A., ²Children's Medical Center Dallas and University of Texas Southwestern Medical Center, Dallas, TX, U.S.A.

PURPOSE:

Sixty-three percent of adults with gastroesophageal reflux disease (GERD) had childhood reflux symptoms. The duration and severity of GERD correlates to the development of Barrett's esophagus (BE). Bile reflux, in particular, is implicated in the malignant progression of BE. Our previous studies demonstrate that bile salt exposure in a Barrett's adenocarcinoma cell line induces proliferation by activating the PI3 kinase/Akt pathway. However, it is not clear that these findings in cancer cells are applicable to the non-neoplastic cells of Barrett's esophagus. Therefore, we studied the effects of bile on PI3 kinase activation and proliferation in a novel, telomerase-immortalized, non-neoplastic Barrett's cell line.

METHODS:

A human, telomerase-immortalized Barrett's cell line was exposed to the conjugated bile salt glycochenodeoxycholic acid (GCDA) at neutral pH. Proliferation was measured by Coulter counter cell counts and BrdU incorporation ELISA. PI3 kinase activity was inferred from Western blots of phosphorylated (active form) and total Akt, the major down-stream effector of PI3 kinase. LY294002, a PI3 kinase inhibitor, was used to block the PI3 kinase/Akt pathway.

RESULTS:

A five-minute exposure to increasing concentration of GCDA, produced a dose dependent cell number increase. Doses of 50uM, 200uM, and 500uM GCDA produced 124%, 132%, and 148% cell number increases (p<0.05), respectively. At the physiologically relevant concentration of bile of 200uM GCDA, a 139% (p<0.05) increase in DNA synthesis was found. Pretreatment with LY294002 blocked all GCDA-induced cell number increase and DNA synthesis, with less than 5% baseline effect of inhibitor alone. With 200uM GCDA exposure, Western blot analysis showed a 2-fold increase in phosphorylated Akt over control within 5 minutes.

CONCLUSIONS:

Conjugated bile salts stimulate proliferation in a non-neoplastic Barrett's cell line in a PI3K dependent fashion. We propose that bile exposure acts as a growth signal in the early stages of non-neoplastic BE, thereby promoting progression to adenocarcinoma.

P8 PHOSPHATIDYLSERINE ON ENDOTHELIUM DERIVED MICROPARTICLES INHIBITS DENDRITIC CELL FUNCTION

<u>John C. Densmore, M.D.</u>¹, Xiao Chen, M.D.¹, Kara Doffek¹, Sonia L. Sugg, M.D.², Keith T. Oldham, M.D.¹, Joel Shilyansky, M.D.¹, ¹Children's Hospital of Wisconsin, Milwaukee, WI, U.S.A., ²Medical College of Wisconsin, Milwaukee, WI, U.S.A.

PURPOSE:

Critically ill patients have impaired ability to clear infection. Elevated plasma levels of endothelium-derived microparticles (EMPs) have been strongly correlated with critical illness (e.g. sepsis, sickle cell disease, and acute lung injury). In a variety of models, we have shown EMP induced endothelial dysfunction affecting NO production, permeability, and inflammation. We hypothesize that EMPs inhibit dendritic cell (DC) maturation, a critical step in immune activation.

METHODS:

Cultured endothelial cells (HUVEC) were treated with plasminogen activation inhibitor and EMPs were isolated from supernatants by differential centrifugation. EMP surface molecules were examined using flow cytometry and Western analysis. To model EMP membranes we generated liposomes comprised of phosphatidylcholine (PC) with or without 30% phosphatidylserine (PS) by extrusion. CD14+ peripheral blood mononuclear cells were treated with GM-CSF and IL-4 to generate DCs. DCs were treated with LPS (100ng/mL) to induce maturation and analyzed 48 hours later. Expression of costimulatory molecules CD80, CD86, and CD83 and production of IL-12p70 were assayed using flow cytometry and ELISA, respectively. DCs were used to stimulate allogeneic CD4+ T lymphocytes. Proliferation was measured using [³H] thymidine incorporation.

RESULTS:

Annexin V is expressed at higher levels on the surface of EMPs compared to HUVECs, suggesting that PS is externalized. We exposed DCs to liposomes as a simplified model of EMPs. In contrast to PC liposomes, PS liposomes inhibited the expression of co-stimulatory molecules (p<0.05) and production of IL-12p70 (p<0.05) by DCs. PS also inhibited the ability of DCs to stimulate the proliferation of allogeneic T cells (p<0.05).

CONCLUSIONS:

Phosphatidylserine is externalized on EMPs and plasma EMP levels are elevated in critically ill patients. Because PS inhibits DC maturation and immunostimulatory function, we suggest that EMPs induce DC dysfunction. This may contribute to the high susceptibility to infection seen in critically ill patients.

P9 ETOPOSIDE ENHANCES TRAIL-INDUCED CYTOTOXICITY IN HUMAN OSTEOSARCOMA <u>Debra K. Doherty, M.D.</u>, Jonathan L. Davies, B.S., Eugenie S. Kleinerman, M.D., Anderson Cancer Center, Houston, TX, U.S.A.

PURPOSE:

Pulmonary metastases remain a major obstacle in the successful treatment of osteosarcoma. Novel therapies need to be developed to treat these recurrent tumors. Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand (TRAIL) is a member of the TNF family of cytokines that causes apoptosis in a variety of cancer cell lines but is generally nontoxic to normal cells. Etoposide is a topoisomerase II inhibitor that has been shown to affect various proteins in the TRAIL pathway. The purpose of these studies was to determine the efficacy of combining TRAIL and etoposide against human osteosarcoma cells.

METHODS:

Four human osteosarcoma cell lines (SAOS-LM7, SAOS-2, MG63, and TE85) were used in these experiments. Flow cytometry demonstrated the presence of TRAIL death receptors (DR4 and DR5) in all four cell lines. Cells were treated for 24 hours with either TRAIL alone (50 ng/ml), etoposide alone (25 μ M), or both drugs in combination. Cell viability was then determined by MTT (methylthiazoletetrazolium) assay.

RESULTS:

Cell lines were sensitive to TRAIL alone *in vitro*, with cell viability following treatment ranging from 24-56% depending on the cell line (Figure). All cell lines were moderately sensitive to etoposide alone, with cell viability after treatment ranging from 42-65%. When both TRAIL and etoposide were administered at the same time, cell viability decreased dramatically (1-12%). Expression of DR4 increased by 45-58% in cells treated with etoposide.

CONCLUSIONS:

These data suggest that etoposide may enhance the activity of TRAIL through the upregulation of death receptors leading to increased cytotoxicity in human osteosarcoma cells. This combination may have a therapeutic benefit in patients with relapsed osteosarcoma.



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Final Program

P10 NOVEL PEPTIDES SECRETED FROM HUMAN NEUROBLASTOMA: USEFUL CLINICAL TOOLS?

John A. Sandoval, M.D., Derek J. Hoelz, Ph.D., Heather A. Woodruff, B.S., Robert L. Powell, B.S., <u>Colleen L. Jay, B.S.</u>, Jay L. Grosfeld, M.D., Robert J. Hickey, Ph.D., Linda H. Malkas, Ph.D., Indiana University School of Medicine, Indianapolis, IN, U.S.A.

PURPOSE:

The identification of proteins differentially expressed by neuroblastoma (NB) is vital for the potential development of new diagnostics, therapeutics and tumor vaccines. As an example, secretory neuropeptides (catecholamines and neuron specific enolase) from human NB have been useful clinically. We investigated NB peptide secretion by employing proteomic technologies to analyze proteins released from NB in culture.

METHODS:

Three human neuroblastoma cell lines (SK-N-AS, SK-N-DZ, and SK-N-FI) grown as monolayers were adapted to serum free media. Conditioned media from each cell line was collected and analyzed for differentially secreted proteins by two- dimensional polyacrylamide gel electrophoresis (2-D PAGE). Selected polypeptides were identified by liquid chromatography linked tandem mass spectrometry (LC-MS/MS).

RESULTS:

Five novel polypeptides were identified that were secreted, shed by membrane vesicles, or externalized by NB cells. Ubiquitin, beta-2 microglobulin, insulin-like growth factor binding protein-2, superoxide dismutase (Cu-Zn), and heat shock cognate 70 kDa protein were differentially secreted from NB cell media as compared to control media. Furthermore, elevated levels of these proteins have been described in serum and tissues under various stressful conditions and in many malignancies, including NB.

CONCLUSIONS:

We identified five novel secretory polypeptides from human NB cell lines. The function of these novel proteins may participate in growth-regulating effects of NB. These secretory proteins may reveal additional tumor markers and permit putative future use of these molecules in the diagnosis and treatment of NB. The ability to detect these proteins in the serum of children with NB vs. healthy controls (using 2-D PAGE and mass spectrometry techniques) is currently in progress.

P11 NEUROBLASTOMAS DO NOT RECUR LOCALLY REGARDLESS OF EXTENT OF TUMOR RESECTION WHEN TREATED WITH THE CHICAGO PILOT II PROTOCOL Marybeth Browne, M.D., Morris Kletzel, M.D., Roopa Seskardi, Susan L. Cohn, M.D., <u>Marleta Reynolds, M.D.</u>, Children's Memorial Hospital, Chicago, IL, U.S.A.

PURPOSE:

Our aim was to investigate the impact of the extent of surgical resection on recurrence in stage IV neuroblastoma patients treated with the Chicago Pilot II protocol.

METHODS:

Retrospective chart review was performed on neuroblastoma patients enrolled in the Chicago Pilot II protocol between 1995-2003. Variables studied were: location of tumor, extent of resection, location of metastases, N-myc amplification, surgical complications, event free survival (EFS), and overall survival (OS). Treatment protocol included: biopsy, induction therapy, surgery for attempted complete resection, three cycles of cyclophos-phamide and stem cell harvest, triple-tandem high dose chemotherapy with PBSC rescue, and radiation to the primary site. Complete resection was defined as no gross residual tumor (primary and lymph node extension).

RESULTS:

Thirty-three patients received surgical procedures at our institution for abdominal neuroblastomas and completed Chicago pilot II protocol treatment. Follow-up was a mean of 4 \pm 2.3 years. EFS was 58% with OS of 56%. Patients with complete resections (CR) (27/33) had an EFS of 52% and OS of 59% compared to patients with incomplete resections (IR) (6/33) who had an EFS of 17% (p=0.1) and OS of 33% (p=0.25) (see Table). Seven patients had nephrectomies with OS of 43% (3/7, p=0.48). Patients who developed recurrent disease (14/33) had a significantly worse OS (3/14, 21%, p= 0.001, OR=6.5). Patients with CR and IR had recurrence rates of 37% (10/27) and 67% (4/6, p=0.18) respectively. Neuroblastoma recurrences were most commonly in bone. One patient with a central tumor and IR recurred locally.

Nominal Variables		# of Patients Total=33	Event Free Survival	p value	Overall Survival	p value
Desection	Complete (CR)	27	14 (52%)	0.1	16 (59%)	0.25
Resection	Incomplete (IC)	6	1 (17%)		2 (33%)	
	Central	5	2 (40%)	0.85	2 (40%)	0.5
Site	Left Adrenal	14	7 (50%)		8 (57%)	
	Right Adrenal	14	6 (43%)		8 (57%)	
Nanhraatamu	Yes	7	3 (43%)	0.87	3 (43%)	0.48
Nephrectomy	No	26	12 (46%)		15 (58%)	
Doourranaa	Yes	14	N/A	N/A	3 (21%)	0.001**
Recurrence	No	19	N/A		15 (79%)	
Nimuo	Amplified	14	7 (50%)	0.7	9 (64%)	0.45
м-ттус	Not Amplified	14	6 (43%)		7 (50%)	

CONCLUSIONS:

Recurrence is a significant determinate of neuroblastoma survival. Tumor recurrence was found outside the primary tumor site regardless of the extent of surgical resection. Final outcome of patients with unfavorable neuroblastoma will be determined by metastatic recurrence not by extent of resection.

Poster Session IB: Clinical Surgery

P12 PEDIATRIC TRAUMA NURSE PRACTITIONERS PROVIDE EXCELLENT CARE WITH SUPERIOR PATIENT SATISFACTION FOR INJURED CHILDREN

<u>Kaaren Fanta, R.N., M.S.N., CPNP</u>, Becky Cook, R.N., M.S.N., CPNP, Crystal Rickets, Ph.D, Lynn Schweer, R.N., M.S.N., CPNP, Richard A. Falcone, Jr., Rebeccah L. Brown, Victor F. Garcia, Cincinnati Children's Hospital Medical Center, Cicinnati, OH, U.S.A.

PURPOSE:

The work hour restrictions mandated for house staff have caused many hospitals to reevaluate their distribution of manpower. At our Level I Pediatric Trauma Center two pediatric trauma nurse practitioners (TNP) have expanded their role to include in patient management. We hypothesized that a TNP can provide mild to moderately injured children a level of care commensurate with a surgical resident (RES).

METHODS:

All injured children between the ages of two months and 17 years admitted to a Level I Pediatric Trauma Center over an eight month period were considered for the study. Patients admitted to the ICU or taken urgently to the operating room were excluded. Patients were randomly divided between TNP and RES care groups based on the day of the week admitted. The care of both groups was supervised by the trauma attending/fellow. Types of injuries, injury severity score (ISS), missed injuries, readmissions, hospital length of stay (LOS) and cost were recorded. Satisfaction surveys were administered to all families.

RESULTS:

A total of 76 children were enrolled, 31 were assigned to the TNP group and 45 to the resident group. During the study period there were no missed injuries or readmissions in either group. The demographic information for both groups was similar (Table 1). The TNP group received significantly higher satisfaction survey scores with regard to information on injuries, tests and treatment, and frequency of visits provided to the patient/family.

	TNP	RES
ISS	4.39 + 0.5	6.60 + 0.7 p=0.08
LOS	19.4 hrs + 2.1	25.4 hrs + 3.1 p=0.26
Cost	\$6319 + 1131	\$6556 + 629 p=0.36

Table 1

CONCLUSIONS:

Trauma nurse practitioners provide equivalent care for injured children with significantly higher patient satisfaction than surgical residents. In-patient trauma nurse practitioners provide added value to the care of the injured child in the era of reduced resident work hours.

P13 SLOW TRANSIT CONSTIPATION-DIAGNOSTIC PITFALLS

Shailinder Jit Singh, M.S., DNB, MCh, FRCS I, FRCS (Eng.), FRCS (Paed.Surg.), Professor Alan Perkins, B.Sc. (Hons), M.Sc., Ph.D., Queen's Medical Centre, Nottingham, United Kingdom.

WITHDRAWN

P14 OUTCOME OF LONGITUDINAL PANCREATICOJEJUNOSTOMY FOR CHRONIC PANCREATITIS IN CHILDREN Jaimie D. Nathan, M.D., Henry E. Rice, M.D., Michael A. Skinner, M.D., Duke University Medical Center, Durham, NC, U.S.A.

PURPOSE:

Chronic pancreatitis is an uncommon disorder in children, and few studies have reported on the surgical management and outcomes of this disease in the pediatric population. We report our institutional experience with longitudinal pancreaticojejunostomy for the management of chronic pancreatitis in children.

METHODS:

We reviewed the medical records of all patients under the age of 18 who underwent longitudinal pancreaticojejunostomy for chronic pancreatitis between 1995 and 2004. Preoperative parameters and clinical course, operative morbidity and mortality, and postoperative symptoms and outcome were examined.

RESULTS:

Six patients were identified, all presenting with intractable recurrent abdominal pain. Etiologies of chronic pancreatitis included one each of post-traumatic pancreatitis, pancreas divisum, hereditary pancreatitis, choledochal cyst, communicating gastric duplication cyst, and idiopathic pancreatitis. Mean preoperative length of symptoms was 1.5 years. All six patients underwent longitudinal pancreaticojejunostomy, and one patient also underwent choledochal cyst excision. Mean age at surgery was 10.8 years (range 0.8 - 16.3 years). There was no surgical mortality and no postoperative complication. Mean postoperative length of stay was 6.8 days (range 4 - 10 days). Over a mean follow-up period of 2.6 years, four patients (67%) have not required postoperative hospitalization for pancreatitis, and three patients (50%) have not had any postoperative episodes of pancreatitis. The postoperative outcome was excellent (no pain; return to normal activity) in two patients, and improved (occasional pain medication) in three patients. One patient required a revision of the longitudinal pancreaticojejunostomy due to intractable recurrent pancreatitis, and her clinical outcome was improved following the revision.

CONCLUSIONS:

We conclude that longitudinal pancreaticojejunostomy for chronic pancreatitis can be performed safely in children. The majority of patients experience improved to excellent clinical outcomes with few postoperative episodes of pancreatitis and limited need for re-hospitalization.

P15 COMPLEX PANCREATIC VASCULAR ANOMALIES

<u>Adam M. Vogel, M.D.</u>, Julia M. Alesbury, Victor L. Fox, M.D., Steven J. Fishman, M.D., Children's Hospital Boston, Boston, MA, U.S.A.

PURPOSE:

Vascular anomalies are vascular tumors and congenital malformations that rarely involve the pancreas. Diagnosis and management of these lesions is complex.

METHODS:

An IRB approved retrospective database and record review from 1994 through 2004 at a quaternary referral center for vascular anomalies was conducted.

RESULTS:

Of 5,051 patients with a vascular anomaly, six had a lesion involving the pancreas. All patients were less than three years of age. There were three tumors (two infantile hemangiomas and one kaposiform hemangioendothelioma) and three malformations (two lymphatic and one venous). The referring diagnoses were correct for four patients. All anomalies were diagnosed with ultrasound, cross-sectional imaging, and/or angiography. Five patients received pharmacologic therapy including two malformation patients who were erroneously treated with anti-angiogenic therapy prior to referral. Two patients with lymphatic malformations underwent operative intervention. Surgery was recommended for the venous malformation. The two infantile hemangiomas were treated with systemic corticosteroid and the kaposiform hemangioendothelioma was treated with a combination of systemic corticosteroid and vincristine. One infantile hemangioma required temporary percutaneous biliary drainage for obstructive jaundice until tumor involution ensued.

CONCLUSIONS:

Pancreatic vascular anomalies are rare. As is generally the case for vascular tumors, endothelial neoplasms of the pancreas are amenable to treatment with anti-angiogenic medications. Operative resection or minimally invasive interventions are reserved for refractory cases or complications. Symptomatic vascular malformations are unresponsive to known drug therapy and require direct interventions such as operative resection. Evaluation and management of pancreatic vascular anomalies is complex and benefits from coordinated interdisciplinary care. Proper diagnosis and classification is essential for formulating an appropriate treatment plan.

P16 PEDIATRIC SHORT BOWEL SYNDROME: WHAT IT ACTUALLY COSTS <u>Ariel U. Spencer, M.D.</u>, Debra Kovacevich, R.N., Deanna Hair, B.A., Michelle McKinney-Barnett, B.S., Christopher Maksym, R.Ph., Daniel H. Teitelbaum, M.D., University of Michigan, Ann Arbor, MI, U.S.A.

PURPOSE:

Care of the pediatric short bowel syndrome (SBS) patient is highly complex, requiring not only hospital care but also sustained home-based care, especially total parenteral nutrition (TPN). The actual total cost of care (COC) for such patients is unknown. This study used the unique construct of our center — providing home care as well as hospital care — to capture the total COC for SBS patients.

METHODS:

All pediatric SBS patients cared for at our center were reviewed. Both in-patient and outpatient charges were abstracted for each patient. COC was the charge billed to the patient and corrected to 2004 U.S. dollars.

RESULTS:

Out of 102 SBS patients cared for over 10 years, total COC could be determined for 39 children. There were 16 males. 21 were diagnosed at day one of life, 10 within two months of life, and the remainder at older ages. Survival was 78%, and 70% weaned from TPN. Duration of home care was 32.7 ± 35.5 months (Mean \pm SD) at a cost of \$352,881 \pm 429,862 per patient. However, inpatient COC per patient was \$432,527 \pm 578,659 over a mean of 137 \pm 188 in-hospital days; and the bulk of charges occurred in the first year of life.

CONCLUSIONS:

The total COC for an SBS patient is quite significant. Although this data may not affect medical decisions, it may provide important information to health care providers and the families of these patients about the financial implications of SBS care. The data may also be useful for comparison with the cost of an intestinal transplant, which has often been viewed as an obstacle because of financial concerns.
P17 THE EFFECT OF A RIGHT SIDED AORTIC ARCH ON OUTCOME IN CHILDREN WITH ESOPHAGEAL ATRESIA

<u>Steven R. Allen, M.D.</u>, Romeo Ignacio, M.D., Richard Falcone, M.D., Maria Alonso, M.D., Frederick Ryckman, M.D., Victor Garcia, M.D., Richard Azizkhan, M.D., Gregory Tiao, M.D., Cincinnati Children's Hospital Medical Center, Cincinnati, OH, U.S.A.

PURPOSE:

The presence of a right sided aortic arch (RAA) presents a technical challenge to the surgeon when repairing an esophageal atresia/tracheoesophageal fistula (EA/TEF). Associated anomalies may further complicate the care and outcome in these patients.

METHODS:

A retrospective review of patients who underwent repair of EA/TEF at our institution from 1990 to 2003 was performed. Fifty-one total patients were identified with a mean length of follow-up of 30.9 ± 7.0 months. Forty-five patients had a left aortic arch (LAA) and six patients had a RAA. We compared clinical presentation, operative approach and outcomes.

RESULTS:

All patients were diagnosed with EA/TEF at birth. The mean gestational age and birth weight was similar between patients with a LAA and those with a RAA. There were significantly more vascular rings identified in the RAA group than in the LAA group (50.0% vs. 4.4%). In addition, more patients with RAA had cardiac malformations than in the LAA group (50.0% vs. 24.0%). Preoperative echo correctly identified the location of the arch in all patients with a LAA but in only 67% of those with a RAA. A right thoracotomy was performed in all patients with a LAA and in 60% of those with a RAA. Of the patients who underwent primary repair, operative complications (chylous leak, recurrent laryngeal nerve injury and anastomotic leak) were four times more frequent in patients with a RAA compared to those with a LAA. Survival was similar in both groups of patients.

CONCLUSIONS:

The management of a child with RAA and EA/TEF is technically challenging. Preoperative identification of the associated great vessel anomalies may impact operative decision making. Although there was no difference in survival, children with RAA suffered considerably more intraoperative complications.

P18 LAPAROSCOPIC APPENDECTOMY WITH AN UMBILICALLY PLACED DUAL-PURPOSE THORACOSCOPIC INSTRUMENT <u>Felix Schier, M.D.</u>, Salmai Turial, M.D., Alexandra Weltzien, M.D., Veronika Engel, M.D., Cordula Scherer, M.D., Jörg Beardi, M.D., University Medical Centre, Mainz, Germany.

PURPOSE:

Considerable controversy remains concerning the preferred approach to appendectomy in children. In this series we analyse a four-year experience with a novel minimal-access technique.

METHODS:

Central to the approach is a dual purpose thoracoscope that consists of an angulated lens system in addition to a parallel 5mm working channel. This versatile instrument is inserted through an umbilically placed 10mm trocar. Additional 1.7 or 2mm instruments (inserted through 12G venous cannulas) or 5mm intruments are added as needed. The appendix is removed through the umbilical trocar. The technique was employed in 248 children (158 girls, 90 boys), aged 6 to 15 years (median 12.8 years), in all stages of appendicitis, except phegmonous masses.

RESULTS:

Median operative time was 45 minutes (35 - 190). Ten cases were converted to the open approach (4%). In ten cases one of the 2mm instruments was replaced by a 5mm instrument (4%). In 14 cases both auxilliary 2mm instruments were exchanged by a 5mm instrument (5.6%). Fifteen pericecal absesses developed (6%); two were evacuated under ultrasono-graphic guidance, the remainder subsided with antibiotics. There were no wound infections or other trocar site complications. Follow up ranged from two to 49 months (median 28 months).

CONCLUSIONS:

This transumbilical approach is an atractive alternative to conventional laparoscopic techniques because in most children it results in a virtually scarless abdomen. Because of the anatomical characteristics of the umbilicus, this technique is particularly attractive for use in overweight children.

P19 THE APPENDIX SIGN: A RADIOGRAPHIC MARKER FOR IRREDUCIBLE INTUSSUSCEPTION

<u>Marion C. W. Henry, M.D.</u>, Christopher K. Breuer, M.D., David Tashjian, M.D., R. Lawrence Moss, M.D., Milissa McKee, M.D., Robert Touloukian, M.D., T. Rob Goodman, Cindy Miller, Jamal Bokhari, Yale University, New Haven, CT, U.S.A.

PURPOSE:

Radiographic reduction of intussusception has become the standard of care in the pediatric population with success rates of over 70%. Identification of those patients who are likely to fail non-operative management could lead to earlier operation, a reduction in radiation exposure, and a decreased risk of complication following repeated attempts at enema reduction. During successful radiographic reduction, the small bowel is almost always visualized prior to the appendix. Visualization of the appendix prior to visualization of the small bowel during a successful reduction of an intussusception is a rare event. We report a new radiographic finding, the appendix sign (radiographic visualization of the appendix without reflux of air or contrast into the small intestine) that is associated with failure of non-operative management.

METHODS:

We performed a retrospective review of the last 12 years of irreducible intussusception cases and identified those with gangrenous bowel that required small bowel resection. These studies were then reviewed to examine the incidence of this radiographic finding.

RESULTS:

Retrospective review of our surgical records demonstrated that between 1992 and 2004 16 cases of intussusception had unsuccessful attempts at radiographic reduction which were followed by exploratory laparotomy and small bowel resection. Nine of these cases had radiographic images suitable for retrospective analysis. Seven of the nine cases (78%) had an unequivocal appendix sign while two cases (22%) were negative for an appendix sign.

CONCLUSIONS:

Our experience suggests that the presence of an appendix sign is associated with failing enema reduction of an intussusception and may be useful as a marker for determining the endpoint for further attempts at radiographic reduction.

P20 INCIDENCE OF PERSISTENT LEFT SUPERIOR VENA CAVA IN ESOPHAGEAL ATRESIA

<u>Nathan Mowery, M.D.</u>, Deborah F. Billmire, M.D., Marcus Shamberger, M.D., Paul Szotek, M.D., Karen West, M.D., Frederick Rescorla, M.D., L. R. Scherer, M.D., Scott Engum, M.D., Tom Rouse, M.D., Jay L. Grosfeld, M.D., Indiana University, Indianapolis, IN, U.S.A.

PURPOSE:

Esophageal atresia is known to be associated with a variety of additional congenital anomalies in multiple organ systems. Emphasis on cardiovascular anomalies has been focused on aortic arch and intrinsic cardiac malformations. Persistent left superior vena cava (PLSVC) is the most common venous thoracic anomaly in the general population and creates a problem when central venous access is required. this review was undertaken to define the incidence of PLSVC in infants with esophageal atresia and to determine if any subgroup of associated anomalies poses additional risk.

METHODS:

A retrospective IRB approved chart review of all children admitted to a children's hospital identified 118 patients treated for esophageal atresia from 1993-2002. Eighty-nine of 118 children had sufficient data for inclusion. Charts were reviewed for gestational age, weight, type of atresia, echocardiogram and associated anomalies. Statistical analysis was performed using the Fisher's exact test.

RESULTS:

Eight of 89 children (9.9%, Confidence Interval 4-17%) had PLSVC compared to the reported incidence of 0.3% in the general population. Presence of additional organ system anomalies did not significantly increase relative risk for PLSVC(Table 1).

CONCLUSIONS:

The incidence of persistent left superior vena cava is significantly increased in children with esophageal atresia when compared to the general population. This increased incidence of PLSVC is not influenced by the presence of cardiac or other associated anomalies. This finding should be kept in mind when central venous access is required in this patient population.

Cardiac Anomaly	4 of 50 (8.0%)	0.73	
No Cardiac Anomaly	4 of 39 (10.2%)		
enal 5 of 31 (16.1%)		1.2	
No Renal Anomaly	3 of 59 (5.1%)	1.2	
Vertebral	2 of 22 (9.1%)	10	
No Vertebral Anomaly	6 of 67 (9.0%)	1.0	
eletal 3 of 25 (12.0%)		0.69	
No Skeletal Anomaly	5 of 64 (7.8%)	0.08	
GI	0 of 17 (0.0%)	0.24	
No GI Anomaly	8 of 72(11.1%)	0.34	
Children with 2 system involvement	0.71		
Children with 3 or more system involvement	6 of 58 (10.3%)	0.71	

P21 THE USE OF ALLODERM[®] IN THE REPAIR OF CEPHALIC FOLD OMPHALOCELE <u>Michael R. Curci, M.D.</u>¹, Albert W. Dibbins, M.D.², Thomas Hamilton, M.D.², Janice Dudley, R.N., PNP², ¹Maine Medical Center, Portland, ME, U.S.A., ²Maine Medical Center, Portland, ME, U.S.A.

The pioneering techniques of Gross and Grob saved the lives of infants with giant omphaloceles but created ventral hernias which required closure. These closures were often difficult. With the availability of synthetic mesh, Schuster and others developed operations to close the defects primarily, but in staged procedures. The use of mesh added to the risk of infection and injury to underlying tissue. We report the use of lyophilized cadaver dermis (Alloderm[®]) in the repair of two cephalic fold omphaloceles; one intact and one ruptured.

In the infant with a ruptured omphalocele, the exposed liver and intestine were covered with Alloderm[®] which was sutured to the margins of the defect. The Alloderm[®] was covered with cadaver skin and subcutaneous tissue expanders were placed in both flanks with the intention of covering the Alloderm[®] with skin flaps. Due to the size of the defect this was not possible. The original cadaver skin has been left in place for 6 months and is slowly separating. The Alloderm[®] remains intact and is slowly contracting.

In the infant with an intact ompahlocele, the membrane was left intact. Alloderm[®] was sutured to the muscular margins of the defect and skin flaps were mobilized under tension to cover the Alloderm[®]. Infection occured beneath the skin flaps which were opened and then retracted. The Alloderm[®] was left in place and was infection resistant. After four months the Alloderm[®] is contracting, reducing the size of the defect and is being epithelialized from the margins. No ventral hernia repair will be required.

Alloderm[®] appears to be the ideal material for coverage of large ventral wall defects which cannot be closed primarily. Because it vascularizes from the underlying tissue, it resists infection, is not rejected, and undergoes contracture as it is replaced by autologous tissue.

P22 EXTRACELLULAR MATRIX DYNAMICS ASSOCIATED WITH TISSUE-ENGINEERED INTRAVASCULAR SCLEROTHERAPY

Adam M. Vogel, M.D., <u>C. Jason Smithers, M.D.</u>, Harry P. Kozakewich, M.D., David Zurakowski, Ph.D., Marsha A. Moses, Ph.D., Patricia E. Burrows, M.D., Dario O. Fauza, M.D., Steven J. Fishman, M.D., Children's Hospital Boston, Boston, MA, U.S.A.

PURPOSE:

An injectable, fibroblast-based engineered construct has been shown to minimize luminal recanalization in a leporine model of vascular sclerotherapy. This study was aimed at determining the effects of this novel treatment on extracellular matrix dynamics.

METHODS:

New Zealand rabbits (n=60) underwent ethanol sclerotherapy of a temporarily occluded jugular vein segment. In controls (n=40), no further manipulations were performed or acellular collagen hydrogel was injected. In tissue-engineered animals (n=20), an autologous fibroblast construct was injected. At 1, 2, 4, and 20-24 weeks postoperatively, sclerosed segments were evaluated for collagen, glycosaminoglycan (GAG), matrix metalloproteinase (MMP) 2 and 9, and tissue inhibitors of matrix metalloproteinase (TIMP) 1 and 2 by special stains or immunohistochemistry. Matrix components were scored on a 0-3 scale based on intensity. Differences between groups and time points were assessed using nonparametric statistical analysis with p<0.05 considered significant.

RESULTS:

Collagen content was significantly higher in animals that received fibroblasts (p<0.05 at all time points; Mann-Whitney U-test). GAG analysis showed a significantly higher grade only at 1 week (p<0.05; Mann-Whitney U-test). Collagen and GAG deposition were prominent at weeks 1 through 4, and diminished by 20-24 weeks. There were no significant differences in MMP 2 and 9, and TIMP 1 and 2 staining between groups. However, significant time-related decreases in grade were seen in MMP 2 and 9 and TIMP 1 and 2 staining (p<0.01; Kruskal-Wallis test).

CONCLUSIONS:

An injectable, fibroblast-based tissue-engineered construct prevents recanalization in this sclerotherapy model (data previously reported). This enhancement of luminal obliteration is mediated, at least in part, by increasing the intraluminal content of collagen and gly-cosaminoglycans. Matrix metalloproteinases and tissue inhibitors of matrix metalloproteinases may play a role in luminal recanalization after experimental vascular sclerotherapy. Tissue engineering may be a valuable adjuvant to sclerotherapy in the treatment of vascular malformations.

Notes:

Poster Session 2A: Basic Science

P23 ABSENCE OF TREFOIL FACTOR 2 ACCELERATES INTESTINAL INJURY IN A MOUSE MODEL OF NECROTIZING ENTEROCOLITIS

<u>Cynthia A. Gingalewski, M.D.</u>, Robert Kiley, M.D., Robert Finberg, M.D., Rhonda Yantiss, M.D., Evelyn Kurt-Jones, Ph.D., University of Massachusetts, Worcester, MA, U.S.A.

INTRODUCTION:

Necrotizing enterocolitis (NEC) remains a devastating disease affecting the premature infant. Despite advances in surgical therapy, our understanding of the pathophysiology of the disease has significantly lagged. The common denominator in the initiation of NEC is a break in intestinal mucosal integrity. Trefoil factor 2 (TFF2) is a mucin-associated peptide present in the intestine and spleen. Its absence is associated with other inflammatory gastrointestinal diseases such as gastric ulcers, and Crohn's disease. This has prompted us to look at the role of TFF2 in a mouse model of intestinal injury.

METHODS:

Wild type (B6129) and TFF2 knockout mice (SPKO) underwent total midgut ischemia by clamping the superior mesenteric artery for 30 minutes. The intestine was then allowed to reperfuse and the animals were given *ad lib* access to food and water. Mice were sacrificed at 1, 4, 12, 24, 48 and 72 hours and intestinal samples were taken for histological assessment. In addition, serum was obtained for cytokine levels. Mice were then followed for overall survival.

RESULTS:

Thirty minutes of ischemia was nonlethal in B6129 mice. In marked comparison, SPKO mice had an 80% mortality within 72 hours. Additionally, the intestinal injury seen was more severe (Grade 4 vs 2) and occurred in as little as 60 minutes after reperfusion. The elevation of serum cytokine levels (IL-6, MCP-1) was prolonged in SPKO mice.

CONCLUSIONS:

A break in the mucosal barrier of the intestine is an important initial event in the development of NEC. Lack of the mucin-associated protein, TFF2, accelerates the intestinal injury seen in the mouse after intestinal ischemia. The lack of TFF2 also produces prolonged elevation of inflammatory cytokines after intestinal injury. The lack of TFF2 may be an important initial event in the development of inflammatory intestinal diseases, such as ischemia/reperfusion and NEC.

P24 THE ROLE OF TOLL LIKE RECEPTOR-4 IN THE PATHOGENESIS OF NECROTIZING ENTEROCOLITIS

<u>Cynthia L. Leaphart, M.D.</u>, Matthew Rivenburgh, B.S., Matthew D. Neal, B.S., Selma Cetin, M.D., Jun Li, Henri R. Ford, M.D., David J. Hackam, M.D., Ph.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

PURPOSE:

Necrotizing enterocolitis (NEC) is the most lethal gastrointestinal disorder of newborns, and results from the translocation of lipopolysaccharide (LPS) into the systemic circulation. The mechanisms governing bacterial translocation across the normally impermeant barrier remain poorly understood. We have shown that enterocytes can phagocytose gram negative bacteria via the LPS receptor, Toll Like Receptor-4 (TLR4), although the capacity for enterocytes to undergo phagocytosis during conditions of intestinal inflammation is unknown. Since bacterial translocation is greater during intestinal inflammation, we hypothesized that the pro-inflammatory cytokine interleukin-1 (II-1) would up-regulate the capacity for phagocytosis to occur. Since II-1 is known to increase nitric oxide (NO) release from enterocytes, we further sought to define a role for NO in enterocyte phagocytosis.

METHODS:

To assess phagocytosis, IEC-6 cells were incubated with fluorescein-biotin labeled E.coli (2h,37C)±the actin stabilizer cytochalasinD ± LPS(50µg/ml), anti-TLR4(20µg/ml), or a non-specific IgG then examined by confocal microscopy in the presence of rhodamine-streptavidin, which excludes extracellular bacteria. In parallel, cells were treated with interleukin-1(100 IU/ml) or the nitric oxide inhibitor L-Nil (10 µM).

RESULTS:

IEC-6 cells were capable of internalizing bacteria in an actin dependent manner (rates of phagocytosis: control: $6\pm 2\%$, CytoD: $0.1\pm .4\%$, p<0.05). Inhibition of TLR4 reduced phagocytosis (control: $7\pm 1\%$, anti-TLR4: $0.5\pm .5\%$, IgG: $6\pm 1\%$, p<0.05). Strikingly, pre-treatment of cells with interleukin-1 significantly increased the rates of phagocytosis, which could be reversed by inhibiting the production of nitric oxide (control: $6\pm 1\%$, IL-1: $11\pm 2\%$, IL-1+L-Nil: $7\pm 2\%$, p<0.05).

CONCLUSIONS:

The proinflammatory cytokine interleukin-1 is capable of increasing the rate of TLR4-dependent bacterial phagocytosis by enterocytes in a nitric oxide dependent manner. This novel pathway could participate in bacterial translocation during intestinal inflammation, and suggests a role for nitric oxide reducing strategies in the management of diseases such as NEC.

Notes:

P25 THE INNATE IMMUNE SYSTEM: ONTOGENY OF THE TOLL-LIKE RECEPTOR Cynthia A. Gingalewski, M.D., <u>Robert Kiley, M.D.</u>, Evelyn Kurt-Jones, Ph.D., Robert Finberg, M.D., University of Massachusetts, Worcester, MA, U.S.A.

PURPOSE:

Infectious complications remain a major cause of morbidity and mortality in premature infants. These infants rely upon their innate immune response as the major defender of microorganisms. This response is mediated by the toll-like receptors (TLRs). TLRs are pattern recognition receptors, thus recognize a wide host of bacteria via a select few receptors. To determine if premature infants are more susceptible to infection because they lack TLRs we studied the ontogeny of the TLRs in the mouse by RT-PCR.

METHODS:

C57/BL6 mice were paired, and female mice were monitored daily for vaginal plugs. Mice were sacrificed at E9, 11, 12, 13, 15, 17, 19, 21, and at 1 week of life. Embryos were harvested and the intestinal tract was separated and total RNA was isolated. Intron spanning RT-PCR primer sets were used for TLR 1, 2, 4, 6 and 9. PCR products were run on 2% TAE gels and the presence of bands were nonquantitatively analysed for the presence of the TLRs throughout gestation.

RESULTS:

RT-PCR was performed on intestinal specimens from embryos and 1 week mouse pups. The presence of TLR1, 2, 4, 6 and 9 were detected in intestine throughout embryogenesis. TLR6 and 9 expression in intestine was lost by 1 week of life, while the remaining TLRs remained expressed in 1 week old pups.

CONCLUSIONS:

The innate immune response is the first line defense against pathogens and this response is mediated by the TLRs. TLR 1, 2, 4 and 9 recognize various gram positive and gram negative bacteria while TLR6 recognizes fungi. These highly conserved receptors appear early in development in the gastrointestinal tract of the mouse. It remains to be determined if the TLRs appropriately bind to bacterial products and initiate the innate immune response.

P26 EFFECTS OF PEROXYNITRITE ON MAPK ACTIVATION IN ENTEROCYTE APOPTOSIS Lydia Stephenson, B.A., Sarah Steinhauser, B.S., Xiaru Zhang, M.D., Dilhari Delamedia, B.A., Henri R. Ford, M.D., Anatoly Grishin, Ph.D., Jeffrey S. Upperman, M.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

PURPOSE:

Intestinal barrier failure in NEC results in part from enterocyte death due to over production of nitric oxide (NO) and reactive nitrogen species. We hypothesize that mitogen activated protein kinases (MAPK), cellular stress molecules, may in part mediate enterocyte apoptosis.

METHODS:

Newborn rats were either subjected to 10 min. of hypoxia (5% O2, t.i.d.) and fed a conventional formula by gavage (NEC), or were breast-fed without hypoxia (BF). Rats were sacrificed on day 0 thru four (n=3/day), and the distal ilea were harvested for total RNA, protein and morphological studies. Total RNA underwent cDNA microarray analysis (27 arrays) and data were analyzed with dChip software. Gene expression was validated with Western analysis. In order to test the role of p38, JNK, and ERK MAPK in enterocyte apoptosis, IEC-6 cells were exposed to peroxynitrite (ONOO) (50 uM) and MAPK activation was detected with Western analysis. Apoptosis was measured with or without SB, an inhibitor of p38 MAPK or SP, a JNK inhibitor. Cells were analyzed for apoptosis (morphology, flow cytometry). Data expressed mean \pm SEM, ANOVA, p<.05.

RESULTS:

NEC groups showed a decrease in barrier integrity compared to BF controls. GADD-45, a p38 activation target, showed 3.3-fold increase compared to BF controls in the microarray (p<.05). GADD-45 immunoblot showed 1.2-fold increase in protein in NEC compared to BF controls. *in vitro*, we found that ONOO upregulated p38 and JNK but downregulated ERK phosphorylation. IEC-6 cells exposed to ONOO/SB (18.6 \pm 1.1%) produced a significant decrease in apoptosis when compared to ONOO alone (40.5 \pm 3.8%)(*p<.05); SP, a JNK inhibitor had no effect(Graph). Histology confirmed our FACS results(d.n.s).

CONCLUSIONS:

These data support the notion that MAPK play a key role in mediating enterocyte apoptosis in NEC. Further studies are needed to elucidate the pathway and substantiate the potential of p38 as a therapeutic target.



Underlining denotes the author scheduled to present at the meeting.

P27 NITRIC OXIDE IMPAIRS ENTEROCYTE MIGRATION THROUGH INACTIVATION OF THE SMALL GTP PROTEIN RAC1

<u>Selma Cetin, M.D.</u>, Cynthia Leaphart, M.D., Jun Li, R.N., Henri R. Ford, M.D., David J. Hackam, M.D., Ph.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

PURPOSE:

Necrotizing enterocolitis (NEC) is characterized by mucosal injury and the release of nitric oxide (NO). Mucosal healing occurs through intestinal restitution, in which enterocytes migrate along the crypt-villus axis which requires actin polymerization and lamellipod extension at the leading edge. In many cells, lamellipod extension requires the activity of the small GTP protein Rac1. We have shown that intestinal restitution is impaired in experimental NEC, although a link between NO, Rac1 and actin remains unproven. We therefore hypothe-sized that NO impairs enterocyte migration by inactivating Rac1 and altering cytoskeletal morphology.

METHODS:

Enterocyte migration was recorded as IEC-6 enterocytes moved into a scraped wound using video microscopic imaging \pm the NO donor detaNONOate (50µM). Rac1 activation was detected as the ability of active Rac1 to interact with the effector protein p21 activated kinase 1 (PAK1) conjugated to glutathione beads. Lamellipod extension and cell morphology were assessed using 3-dimensional cellular reconstructive software (Metamorph). Actin polymerization was measured by detecting the spectral shift of pyrene conjugated actin \pm NO using a fluorescence spectrophotometer (Excitation 365/Emmission 410 nm), and in rhodamine-phalloidin stained IEC-6 cells imaged with confocal microscopy. Data =means \pm SEM.

RESULTS:

NO significantly impaired enterocyte migration in a dose dependent manner (ctrl 17 ± 2 vs NO 4µm/h, p<0.05), and decreased activation of Rac1 (see Figure). Actin polymerization was significantly enhanced by NO (fluorescent units/second control: 100 ± 15 vs. NO: 200 ± 25 , p<0.05) although lamellipod extension was not concomitantly increased (control: 10 ± 3 vs. NO 9 ± 2 µm , p=0.2). Accordingly, NO-treated enterocytes acquired an actin rich, cuboidal phenotype and could not extend a lamellipod for movement.

CONCLUSIONS:

Nitric oxide inhibits enterocyte migration by inactivating Rac1, leading to alterations in cytoskeletal architecture. This provides evidence of a role for Rac1 as a target governing impaired mucosal healing in the pathogenesis of necrotizing enterocolitis.



P28 DISTENSION ENTEROGENESIS: INCREASING INTESTINAL SIZE AND FUNCTION <u>Devin Puapong</u>¹, Benjamin Wu², James Atkinson², James Dunn², ¹Kaiser Permanente, Los Angeles, CA, U.S.A., ²University of California Los Angeles, Los Angeles, CA, U.S.A.

PURPOSE:

The purpose of this study is to evaluate the feasibility of using mechanical force to lengthen small bowel while preserving intestinal enzymatic function.

METHODS:

Male Sprague-Dawley rats had a 3 cm jejunal segment taken out of continuity. A catheter was inserted in the proximal end and the distal end was oversewn. Continuous infusion of saline (0.2 cc/hour) into the isolated loop was started two weeks postoperatively. Segments were harvested one week later. Segment weights and lengths were measured preoperatively and at the time of harvest. Histology of harvested segments was performed. Alkaline phosphatase (ALP) and lactase assays were performed. Comparisons were made with normal jejunum from control animals. Experiments were performed in triplicate on three separate pieces from each segment. Statistical significance was determined using a student's t-test.

RESULTS:

Distended segments (n=7) exhibited hypertrophy of the smooth muscle layers and preservation of villi length upon histological comparison with control segments (n=7). Segment length following distension increased from 3.09 + .32 cm to 4.11 + .69 cm, a significant increase of 33% (p = .01). The ratio of weight to length for distended segments was significantly greater than control segments (.38 + .22 vs. .08 + .005 g/cm; p = .02), however, the ratio of total protein to weight remained similar in the two groups. ALP specific activity was not affected by distension, however, due to the increase in size, total segment ALP activity was significantly higher in experimental animals as shown below. Similar results were obtained for lactase activity.

CONCLUSIONS:

Mechanical force appears to be a viable method for increasing small intestinal length without compromising enzymatic function. This phenomenon may provide a new method for the treatment of patients with short-bowel syndrome in the future and further study is warranted.



P29 ONTOGENY OF SODIUM-GLUCOSE CO-TRANSPORTER-1 (SGLT-1) IN A FETAL RABBIT MODEL OF INTRAUTERINE GROWTH RETARDATION (IUGR) <u>Christina Cellini, M.D.</u>, Jian Xu, M.D., Terry L. Buchmiller-Crair, M.D., Children's Hospital of NY Presbyterian-Weill Cornell Medical College, New York, NY, U.S.A.

PURPOSE:

Premature and IUGR infants have impaired GI function with feeding difficulties and predisposition to NEC. The rabbit provides a naturally occurring model of IUGR based on uterine position. SGLT-1 is a membrane protein responsible for carbohydrate transport across the intestinal brush border and is the primary glucose transporter utilized after birth. Previous studies demonstrate decreased small intestine (SI) dissacharidase expression and nutrient uptake in IUGR fetal rabbits. However, fetal SGLT-1 expression is unknown. We hypothesized that SGLT-1 is present during the last trimester, and that intrinsic differences in native SGLT-1 expression are present between normal and IUGR fetuses.

METHODS:

Nineteen fetal rabbit pairs (Normal vs. IUGR) were harvested on gestational day 23, 25, 27, 29, or 31 (term) and the SI (proximal, middle, distal) removed. RT-PCR measured SGLT-1 /GAPDH mRNA densitometric band ratios for each intestinal region. Statistical analysis was performed using the paired Student's t-test.

RESULTS:

Fetal weights were decreased in IUGR fetuses commencing from day 25 to term (p<0.05) supporting this model of IUGR. From day 23 to 27 IUGR fetuses expressed equal or decreased SI SGLT-1 mRNA levels compared to Normals. SGLT-1 mRNA peaked on Day 29 (Normal, p=0.04; IUGR, p=0.07) and trended higher in the distal SI in IUGR vs. Normals. SGLT-1 mRNA levels decreased to earlier levels by day 31 with IUGR>Normal. Trends were uniform throughout the intestine, without significant regional variation.

CONCLUSIONS:

We conclude that native differential patterns in the expression of SGLT-1 exist between normal weight and IUGR fetuses throughout the last 1/3 of gestation. Initially, SGLT-1 mRNA expression in IUGR fetuses lagged behind that of normal fetuses, which then surpassed normal fetus mRNA expression from day 29 to term. These findings parallel previously reported delayed SI dissacharidase expression and nutrient uptake in the IUGR fetus.



Underlining denotes the author scheduled to present at the meeting.

P30 NF-kB NEGATIVELY REGULATES LIPOPOLYSACCHARIDE SIGNALING IN ENTEROCYTES VIA INDUCTION OF MKP1 PHOSPHATASE <u>Anatoly V. Grishin, Ph.D.</u>, Jin Wang, M.S., Athalie Young, David J. Hackam, M.D., Ph.D., Jeffrey Upperman, M.D., Ruben Zamora, Ph.D., Henri R. Ford, M.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

PURPOSE:

Necrotizing enterocolitis (NEC), a life-threatening gut inflammation in the pre-term neonates, is associated with the exposure of immature intestinal epithelium to bacteria and their toxins such as lipopolysaccharide (LPS). We hypothesized that the limited ability of the immature intestinal epithelium to develop tolerance to LPS may be an important factor in the pathogenesis of NEC. To test this hypothesis, we sought to identify mechanisms of LPS tolerance in enterocytes. Because mitogen-activated protein kinases (MAPK) mediate various responses to LPS, we reasoned that LPS-induced expression of MAPK deactivating phosphatases such as MKP1 might be one of the mechanisms of LPS tolerance.

METHODS:

IEC-6 rat intestinal epithelial cells were treated with 5 μ g/ml LPS for 0-120 min. Activation of MAPK and the expression of MKP1 were examined by immunoblots. ERK, JNK, and p38 MAPK cascades were inhibited by specific pharmacologic inhibitors or expression of dominant-negative constructs. NF- κ B pathway was inhibited pharmacologically or by dominant-negative inhibitory I κ B subunits. Protein and mRNA synthesis were inhibited by 10 μ g/ml cycloheximide and 5 μ g/ml actinomycin D.

RESULTS:

LPS caused rapid but transient activation of ERK, JNK, and p38. p38 activation was sustained in cells pre-treated with cycloheximide or actinomycin D, indicating that new protein synthesis is required for deactivation. LPS-induced MKP1 protein expression peaked at 15-30 min, closely following the peak of p38 activation (15 min). LPS-induced MKP1 expression was abrogated by Bay11-7082, a specific inhibitor of I κ B kinase, NF- μ B inhibitory peptide SN50, or dominant-negative I κ B, but not by specific inhibitors or dominant-negative mutants of ERK, JNK, or p38 pathways.

CONCLUSIONS:

One of the mechanisms of LPS tolerance in enterocytes is NF-ÎB-mediated expression of the MKP1 phosphatase. Studies of this negative regulatory cascade may provide new insights into the pathogenesis of NEC.

Notes:

P31 HEPATIC OVAL CELLS AND WNT SIGNALING <u>Masashi Kurobe</u>, Yue Xu, Brett Staahl, Roel Nusse, Karl G. Sylvester, M.D., Stanford University, Stanford, CA, U.S.A.

PURPOSE:

Hepatic progenitor (oval) cells are thought to possess bipotent differentiation capabilities for both hepatocyte and bile duct epithelium (BDE). Oval cells proliferate from the portal triad in the hepatic lobule during chronic liver injury, when hepatocytes are unable to replace damaged parenchyma. The mechanism of oval cell proliferation and migration remains unknown. Since Wnt signaling is a known critical regulator of progenitor cell biology, the objective of this study was to determine the role of Wnt signaling in oval cell proliferation, migration, and differentiation during chronic liver injury.

METHODS:

A 3,5-diethoxycarbonyl- 1,4-dihydrocollidine (DDC)- enriched diet was used to stimulate oval cell proliferation in a mouse model of chronic liver injury. Control animals were fed a normal diet. Livers were harvested at various time points for histological assessment. RT-PCR was used to assess the Wnt family gene profile. Transgenic mice with a TCF/LEF response element were utilized to identify Wnt responsive cells.

RESULTS:

Oval cells were observed to proliferate increasingly from the portal triads after t=1,2,3, and 4 weeks of DDC stimulation. Areas of atypical ductal hyperplasia stained with β -galactosidase indicating the proliferating cells were Wnt/ β -catenin responsive. Wnt7a and Wnt10a were induced between 1 and 4 weeks in DDC fed mice, but not in control mice. Wnt4 and Wnt5a were consistently detected in both control and DDC fed mice at all time points.

CONCLUSIONS:

What signaling seems to play a significant role in the regulation of the progenitor oval cell response in the liver subject to chronic injury. Ongoing experiments are focused on further defining the specific role of each of the identified Whats and respective signaling mechanisms.

P32 ANORECTAL MALFORMATION IN EPHRIN-B2^{LACZ/LACZ} MUTANT MICE* <u>Nilda M. Garcia, M.D.</u>, M E. Martinez, M.S., C. Dravis, M.S., D. Vasquez, M.D., M. Henkemeyer, Ph.D., Linda Baker, M.D., UT Southwestern Med Center, Dallas, TX, U.S.A.

*Authors received grants/research support from NIH.

PURPOSE:

Knowledge of anorectal embryonic development is limited despite the frequency of anorectal malformations (ARM) in humans. The Eph family of receptor tyrosine kinases and their ligands, the ephrin family, mediate diverse cell-cell recognition events, including neuronal axon pathfinding, neural crest cells migration and vasculogenesis. Our group (Dravis et al, Dev Biol, 2004) reported that ephrin-B2^{lacZ/lacZ} mice manifest high imperforate anus in males and persistent cloaca in females. Ephrin-B2 is expressed in the developing urogenital sinus and hindgut epithelium. Other mutant mouse models, including mice null for the transcription factors Sonic Hedgehog (Shh) or Gli-3, also manifest ARM. In this study, we investigated whether altered ephrin-B2 signaling affects the protein expression of Shh or Gli-3 in the developing anorectum of our ephrin-B2^{lacZ/lacZ} mutant mice.

METHODS:

Embryonic day 11.5 fetal mouse littermates were used. Wild type, heterozygous ephrin-B2^{lacZ/+}, and homozygous ephrin-B2^{lacZ/lacZ} mice were sexed, fixed in 4% paraformaldehyde, wax embedded, sectioned and mounted on slides. Immunohistochemistry for Shh and Gli-3 was performed with diaminobenzedine detection. Control sections were performed with no primary antibody.

RESULTS:

In WT male mice, Shh and Gli-3 protein immunolocalizes to the epithelium of the anorectum. In WT mice, Gli-3 was most abundant within the epithelial edge of the urogential sinus. In ephrin-B2^{lacZ/lacZ} male mice, septation did not occur and Shh localization did not appear altered from WT controls. In contrast, Gli-3 appeared intensified in the epithelium of the fistulous connection of the anorectum with the urogential sinus when compared to the WT controls.

CONCLUSIONS:

During embryonic cloacal and hindgut development, Shh protein localizes normally while epithelial Gli-3 protein is moderately increased at the midline edge of the urorectal septum in ephrin-B2^{lacZ/lacZ} mutant mice. Further study of this novel model of anorectal malformation will deepen our understanding of the molecular basis of anorectal development.

Notes:

Poster Session 2B: Embryology, Fetal Surgery and Tissue Engineering

P33 NDSP IS A NOVEL NERVE GROWTH FACTOR RESPONSIVE GENE.

Sanjeev A. Vasudevan, M.D.¹, Kuan Wang, M.D., Ph.D.², Susan M. Burlingame¹, Jianhua Yang, Ph.D.², Jed G. Nuchtern, M.D.³, ¹M.E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX, U.S.A., ²Texas Children's Cancer Center, Department of Pediatrics, Baylor College of Medicine, Houston, TX, U.S.A., ³M.E. DeBakey Department of Surgery, Texas Children's Cancer Center, Department of Pediatrics, Baylor College of Medicine, X, U.S.A.

PURPOSE:

We have previously described the initial cloning and characterization of neuroblastoma derived secretory protein (NDSP). Because NDSP is actively secreted by neuroblastoma, we tested the hypothesis that NDSP synthesis and secretion may be stimulated by growth factors and cytokines involved in neuroblastoma tumorigenesis.

METHODS:

SH-SY5Y (neuroblastoma cell line) cells exposed to a set of growth factors and cytokines including: TGF- β (5, 10 ng/ml), IGF-1 (10, 100 ng/ml), TNF- α (10, 20 ng/ml), IL-1 β (10, 20 ng/ml), BDNF (10, 100 ng/ml), and NGF- β (10, 100 ng/ml). Cells were incubated for 48 hours and lysed for RNA extraction. Real-time quantitative PCR was performed and analyzed using the comparative C(t) method. PC-12 cells were treated with NGF- β (50 ng/ml) and cells were lysed at four time points (0, 4, 8, and 16 hours). NDSP protein levels in SH-SY5Y supernatant were tested with Western.

RESULTS:

NDSP mRNA expression in SH-SY5Y cells minimally increased above control with IGF-1, TNF- α , and IL-1 β treatment. TGF- β and BDNF resulted in a decrease in NDSP mRNA levels. The most dramatic increase (3-3.5 fold) in NDSP transcript level was seen in a dose responsive fashion with NGF- β . Because PC-12 cells are extensively used as a model for NGF and trk-A/p75 signaling, we chose to treat these cells with NGF- β and test NDSP transcript levels. NDSP mRNA expression increased to seven-fold above control after eight hours of treatment and remained at this level after 16 hours. Having established a correlative increase in NDSP mRNA with NGF- β , we tested the effects on NDSP protein secretion in neuroblastoma. SH-SY5Y treated with NGF- β had a significant increase in NDSP protein secretion.

CONCLUSIONS:

NDSP mRNA and protein levels are responsive to NGF- β . This finding helps to establish NDSP as a potential mediator of tumor growth in neuroblastoma.

P34 THREE DIMENSIONAL COMPUTERIZED THORACIC VOLUME RECONSTRUCTION FROM TWO DIMENSIONAL RADIOGRAPHS: A NEW TECHNIQUE FOR CDH PATIENTS

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PURPOSE:

We have previously reported long term follow-up for a group of severe congenital diaphragmatic hernia patients. Oxygen supplementation at hospital discharge identified a subset of patients at highest risk for neurodevelopmental delay. Unfortunately, formal pulmonary function testing cannot be performed in this age range of patients. In addition, thoracic volume imaging by CT scan frequently requires sedation or general anesthesia, a less than desirable alternative in this patient population. The purpose of this study was to utilize a previously published technique, constructing three dimensional lung volumes from two dimensional plain radiographs, to evaluate thoracic volume in this group of patients.

METHODS:

Institutional approval was obtained. The patients in this study were previously enrolled in a randomized NIH trial. Plain radiographs were obtained at one and two years of age. Digital copies of these radiographs were used to perform computerized reconstruction and subsequent thoracic volume measurements (Rhino, Seattle, WA). Data was plotted against a nomogram of sex and age matched control patients. These volume measurements were then compared to physiologic pulmonary function measurements taken at discharge, one, and two years of age.

RESULTS:

1) As shown in Figure 1, three dimensional lung volume measurements were obtained and comparable to age and sex matched controls. 2) A trend toward patients at highest risk (those requiring oxygen at hospital discharge) was identified, as they had the smallest measured lung volumes.

CONCLUSION:

Three dimensional thoracic reconstructions of two dimensional radiographs provide an additional means of quantifying pulmonary development. This technique is particularly useful in the pediatric population in whom physiologic tests are difficult. Further studies are required to evaluate these findings.

(graphic on next page)



Figure 1: Three dimensional reconstruction of two dimensional radiographs. (A) Digital image of A/P chest radiograph incorporated into Rhino computer-modeling program. (B) A wire frame model is erected with circumferential cross-sectional curves intersecting with the boundaries of the lungs at 0.5 cm intervals. (C) Volumetric measurements of ten CDH patients at approximately one and two years of age plotted on a nomogram of age and sexmatched control patients (nomogram data derived from volumetric reconstruction of computerized tomography scans).

P35 MR SPECTROSCOPY FOR EVALUATING FETAL LUNG MATURITY

<u>Matthew S. Clifton, M.D.</u>, Bonnie N. Joe, M.D., Ph.D., Mark Swanson, Ph.D., Andrew Zektzer, Ph.D., John Kurhanewicz, Ph.D., Daniel B. Vigneron, Ph.D., Fergus Coakley, M.D., Robert Ball, M.D., Amy J. Wagner, M.D., Raul A. Cortes, M.D., Erich J. Grethel, M.D., Vickie Feldstein, M.D., Kerilyn K. Nobuhara, M.D., University of California, San Francisco, San Francisco, CA, U.S.A.

PURPOSE:

Amniocentesis is an invasive procedure with inherent risks to a mother and her fetus. Magnetic Resonance (MR) spectroscopy is a non-invasive, safe way of assessing levels of choline containing compounds (including surfactant). The purpose of this study is to develop a non-invasive technique for assessing fetal lung maturity *in vivo* using Magnetic Resonance Imaging (MRI) by demonstrating differences in amniotic fluid choline concentrations between the second and third trimester.

METHODS:

This study was approved by the Committee on Human Research. MR spectroscopy was performed on *ex vivo* samples of amniotic fluid from second and third trimester fetuses. *In vivo* magnetic resonance spectroscopy was performed on amniotic fluid and fetal lungs in third trimester fetuses. Spectral acquisition and analysis was performed by an attending radiologist in conjunction with an MR spectroscopist.

RESULTS:

Spectra obtained from third-trimester amniotic fluid processed *ex vivo* showed that choline containing compounds (including surfactant) are observed from 3.20 - 3.25 ppm. *Ex vivo* specimens from fresh and frozen samples yielded nearly identical spectra. Spectra obtained from third trimester amniocentesis show a trend toward an increased quantity of choline when compared with those from the second trimester. Spectra obtained from amniotic fluid and lungs of a third trimester fetus (Figure 1) show that choline can be detected in the *in vivo* setting.

CONCLUSIONS:

- 1. MR spectroscopy is a safe, non-invasive procedure.
- 2. MR spectroscopy can measure choline levels in fetal lung and amniotic fluid.
- 3. MR spectroscopy shows a trend toward increased quantity of choline in the third versus second trimester amniocentesis.
- 4. Snap-frozen amniotic fluid yields spectra identical in appearance to its matched, fresh counterpart.

(graphic on next page)



Figure 1. In vivo MR spectroscopy for fetal lung maturity in a 37-week fetus obtained at 1.5T on a clinical scanner. (a) Localization of spectroscopy voxel within amniotic fluid on a transverse image through the maternal abdomen. (b) Corresponding in vivo spectrum of amniotic fluid demonstrating presence of choline. (c) Localization of spectroscopy voxel within the fetal lung in the same patient on a transverse image through the maternal abdomen. (d) Corresponding in vivo spectrum of fetal lung also demonstrates presence of choline.

P36 HISTOLOGICAL EVIDENCE OF VENOUS OBSTRUCTION IN FETAL EXTRALOBAR PULMONARY SEQUESTRATION ASSOCIATED WITH TENSION HYDROTHORAX <u>Yoshihiro Kitano, M.D.</u>, Toshiro Honna, M.D., Tatsuo Kuroda, M.D., Nobuyuki Morikawa, M.D., Kentarou Matsuoka, M.D., Satoshi Hayashi, M.D., Haruhiko Sago, M.D., National Center for Child Health and Development, Setagaya-ku, Japan.

PURPOSE:

Some cases of fetal extralobar pulmonary sequestration (EPS) are associated with massive pleural effusion (PE) leading to tension hydrothorax and fetal hydrops. The underlying mechanism as well as the origin of the fluid is not well understood. This study was performed to find histological evidence for a hypothesis that venous obstruction is the cause of PE in some EPS.

METHODS:

We recently experienced three cases of fetal EPS complicated with tension hydrothorax requiring thoracentesis and eventually thoracoamniotic shunt placement. Total protein content and cell count was measured in the aspirated fetal PE, which was compared with fetal chylothorax cases (n=5) also requiring shunt placement. After birth, all three infants required EPS removal to control PE. Torsion was not seen in any case. The venous wall thickness was measured on pathology slides stained with Elastica van Gieson staining. Thickness of the media and adventitia were measured in approximately 40 veins (100-1000 um in diameter) per case. They were corrected by external diameter and expressed as % medial thickness (%MT) and % adventitial thickness (%AT). Another case of EPS not associated with pleural effusion but with CDH served as a control.

RESULTS:

Total protein and the cell count of the EPS related PE was 0.57 ± 0.3 mg/dl (mean±SD) and 28 ± 14 /µl, which were significantly lower than those of PE in chylothorax (2.2±0.2 mg/dl and 1900±1100 /µl). %MT and %AT of EPS with PE were 7.0±1.9% and 9.5±3.8%, respectively. They were significantly increased compared with those of EPS without PE (2.3±0.7% and 3.1±1.3%).

CONCLUSION:

PE associated with EPS is transduate rather than lymphatic fluid. The thickened media and adventitia found in EPS with PE supports the hypothesis that venous obstruction leads to increased transduate production, which is the origin of the PE.

(graphic on next page)

Media and Adventitia are thickened in EPS with PE



P37 TRACHEAL OCCLUSION IN FETAL RATS ALTERS EXPRESSION OF MESENCHYMAL NUCLEAR TRANSCRIPTION FACTORS WITHOUT AFFECTING SURFACTANT PROTEIN EXPRESSION

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PURPOSE:

Mesenchymal nuclear transcription factors (MNTF) are involved in lung development and maturation and regulate surfactant protein (SP) expression. Prolonged fetal tracheal occlusion (TO) has been shown to accelerate lung growth and inhibit pulmonary surfactant synthesis. The effect of TO on SP expression and MNTF, however, have not been formally assessed. The objectives of this study were to evaluate the effects of short-term TO on normal lung growth, protein expression of pulmonary MNTF involved in SP synthesis and SP expression (mRNA+protein).

METHODS:

At E19 (term=22 days) two fetuses per time-dated Sprague-Dawley rats (n=19) underwent either TO (n=15) or a sham (n=22) operation. Lungs were harvested 72h postsurgery. Pulmonary SP-A, -B, -C mRNA expression and SP-A and -B, Hox-B5, TTF-1 and RXRa protein expression were analyzed. All experimental protocols were approved by the Institutional Animal Care and Use Committee.

RESULTS:

Lung weight was significantly increased by TO (TO 0.29+0.01g vs. SHAM 0.12+0.01g; p<0.001), resulting in 118.1% increase in lung-to-body-weight ratio. No difference of SP-A-mRNA (TO 177+4.3 vs. SHAM 169+4.4; p=0.25), SP-B-mRNA (TO 87.6+0.2 vs. SHAM 87.4+0.02; p=0.33), and SP-C-mRNA (TO 186.5+3.2 vs. SHAM 183.2+2.7; p=0.45) expression was found. SP-A (TO 174.6+25.3 vs. SHAM 192.5+19.8; p=0.59) and SP-B (TO 165.4+5.8 vs. SHAM 166.8+9.3; p=0.37) protein expression were similar in both groups, however Hox-b5 (TO 70.3+18.9 vs. SHAM 130.6+5.1; p<0.02) and TTF-1 (TO 102.6+19 vs. SHAM 181.1+6.3; p<0.02) protein expression were significantly decreased, whereas RXRa protein expression tended to be increased by TO (TO 171.9+6.0 vs. SHAM 155.4+6.7; p=0.11).

CONCLUSIONS:

Short-term TO late in gestation induces rapid lung growth. SP-mRNA and protein expression, are not significantly altered. However, TO leads to an abnormal expression of MNTF suggesting that duration of occlusion may be important in balancing the effects of TO on lung growth versus lung maturation.

Notes:

P38 EFFECT OF VEGF ON THE BRANCHING MORPHOGENESIS OF NORMAL AND NITROFEN-INDUCED HYPOPLASTIC FETAL RAT LUNG EXPLANTS <u>Masato Shinkai, M.D.</u>, Toko Shinkai, M.D., Sandra Montedonico, M.D., Prem Puri, M.S., FRCS, Children's Research Centre, Our Lady's Hospital for Sick Children, Dublin, Ireland.

PURPOSE:

Vascular endothelial growth factor (VEGF) is a member of the oxygen-sensing pathways which play an important role in embryo development. VEGF expression in the lung is upregulated by pulmonary stretch which induces lung growth. Moreover, vascular abnormalities as well as VEGF downregulation have been reported in hypoplastic lungs associated with congenital diaphragmatic hernia. We hypothesized that VEGF accelerates branching morphogenesis and thus may modulate lung growth in nitrofen-induced pulmonary hypoplasia. We designed this study to evaluate the effect of VEGF on normal lung as well as nitrofen-induced hypoplastic lung explants.

METHODS:

A hypoplastic fetal lung model and a normal control lung model were induced by feeding a pregnant rat with or without nitrofen (100 mg) on day 9.5 of gestation, respectively. Fetal lungs harvested on day 13.5 were cultured in the serum-free medium for 72 hours with exogenous rat VEGF (0, 25, 50, 100 ng/ml) added daily in the culture medium (normal lung n=5, 3, 3, 7; hypoplastic lung n=5, 7, 6, 5). Lung bud count was measured under the computer-assisted digital tracings. The increase in bud count was calculated as the ratio of each value at 72 hr minus each value at 0 hr, divided by the value at 0 hr.

RESULTS:

Lung bud count were significantly increased in normal lung incubated with 50, 100 ng/ml VEGF compared to controls $(2.5\pm0.3, 2.8\pm0.3 \text{ vs } 1.5\pm0.6)$ (p<0.05). Moreover, lung bud count were significantly increased in nitrofen-induced hypoplastic lung incubated with 25, 50, 100 ng/ml VEGF compared to controls $(2.7\pm0.2, 2.0\pm0.5, 2.4\pm0.3 \text{ vs } 1.2\pm0.2)$ (p<0.05).

CONCLUSIONS:

This study demonstrates that VEGF accelerates branching of both normal and nitrofen-induced hypoplastic fetal lung explants. These data suggests that VEGF plays an important role in lung morphogenesis and may accelerate lung growth in nitrofen-induced hypoplastic lung.

P39 GENE EXPRESSION PROFILE OF THE WNT FAMILY IN CRANIAL SUTURE DEVELOPMENT <u>Preeti Malladi, M.D.</u>, Yue Xu, M.D., Ph.D., Roel Nusse, Ph.D., Michael T. Longaker, M.D., M.B.A., Stanford University, Stanford, CA, U.S.A.

PURPOSE:

Craniosynostosis, the premature fusion of cranial sutures, can result in abnormal skull morphology and severe functional disorders in children. Various growth factors, such as FGF-2 and the TGF-beta family, and the paracrine effects of the underlying dura mater have been implicated in suture fusion. The WNTs, a family of 19 proteins, are thought to be powerful regulators of patterning, growth, and homeostasis during embryogenesis and carcinogenesis. However, their biological role in suture development has yet to be elucidated.

METHODS:

The mouse posterior-frontal (PF) suture, which lies along the midline of the calvarium, fuses postnatally; whereas the immediately adjacent sagittal (SAG) suture does not. For this experiment, the PF and SAG sutures were carefully dissected from juvenile (< five-day-old) and adult (three- to four-week-old) FVB mice; and the underlying dura mater was meticulously separated. RNA extraction, reverse transcription, and PCR were performed on the samples. WNT family gene expression patterns were examined.

RESULTS:

WNT4 and WNT5a were uniformly expressed in all four components. WNT1, which has rarely been reported in postnatal tissue, was expressed in both sutures in juvenile animals but not in adults. The most striking finding was that WNT 3a showed abundant expression only in the SAG dura mater in juvenile animals. It was not expressed in the sutures and PF dura mater or in adult animals.

CONCLUSIONS:

This experiment reveals that the WNTs are differentially expressed in cranial sutures. In addition, WNT3a, which has been shown to enhance proliferation of mesenchymal cells and inhibit osteogenesis, may play a role in maintaining the patent suture. This interesting finding will be further investigated through *in vitro* and *in vivo* experiments.

P40 CARTILAGE ENGINEERING FROM MESENCHYMAL AMNIOCYTES: POSSIBLE APPLICATION IN THE TREATMENT OF CONGENITAL TRACHEAL ANOMALIES <u>Shaun M. Kunisaki, M.D.</u>, M.Sc., Russell W. Jennings, M.D., Dario O. Fauza, M.D., Children's Hospital Boston, Boston, MA, U.S.A.

PURPOSE:

The treatment of severe congenital tracheal anomalies remains largely unsolved. Fetal mesenchymal cells normally found in the amniotic fluid have been shown to differentiate into all mesenchymal phenotypes *in vitro*, except for chondrocytes. This study was aimed at determining whether cartilaginous grafts suitable for tracheal reconstruction could be engineered from these cells.

METHODS:

Ovine mesenchymal cells isolated from the amniotic fluid were expanded in culture and dynamically seeded at a density of 40-80 million cells per cm2 onto tubular-shaped (25 mm length, 8 mm diameter) polyglycolic acid scaffolds (63 mg/mL, 3 mm thickness) treated with 3% poly-L-lactic acid. The engineered constructs (n=5) were maintained in a rotating biore-actor containing serum-free medium supplemented with transforming growth factor beta and insulin growth factor for 10-15 weeks. All specimens were then compared with native fetal hyaline cartilage samples (n=5) by standard and matrix-specific stainings, as well as quantitative assays for glycosaminoglycans, elastin, and collagen type II levels. Statistical analysis was by one-way analysis of variance, with post-hoc pairwise comparisons by Dunnett's test (significance at p<0.05).

RESULTS:

All constructs became firm tubular conduits, with histological evidence of chondrogenic differentiation (Figure). Glycosaminoglycans and elastin levels were similar in the extracellular matrix of engineered constructs and native fetal hyaline cartilage, despite some morphological differences between these two groups on histology. Collagen type II concentrations tended to be lower in the engineered constructs than in native cartilage, however this was not statistically significant in this series.

CONCLUSIONS:

Fetal mesenchymal cells present in the aminotic fluid can be used to engineer three- dimensional, tubular cartilaginous structures potentially suitable for tracheal reconstruction. The amniotic fluid can be a reliable and practical cell source for the engineering of cartilage constructs.



P41 TISSUE ENGINEERING OF THE ADRENAL CORTEX

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PURPOSE:

Adrenal cortical cell transplantation may correct states of adrenal insufficiency. We wish to evaluate different methods of adrenal cortical cell delivery to regenerate adrenal cortical tissues.

METHODS:

Primary adrenal cortical cells were obtained from murine adrenal glands by enzymatic digestion. Isolated adrenal cortical cells were either injected directly under the renal capsule or were seeded on a collagen matrix prior to implantation under the renal capsule. These two modalities of cell delivery were compared to intact adrenal glands that were transplanted under the renal capsule. RNA extracted from the retrieved tissues were analyzed by real-time PCR to determine the levels of adrenal cortical gene expression including SF-1, DAX-1, and 11beta-hydroxylase.

RESULTS:

The direct injection of adrenal cortical cells resulted in regenerated tissues that expressed SF-1, DAX-1, and 11beta-hydroxylase for up to eight weeks after implantation. The expression levels of these adrenal-specific genes, however, were very low as compared to those in the transplanted intact adrenal gland. In contrast, the adrenal cortical cells seeded on a collagen matrix resulted in regenerated tissues that expressed levels of SF-1, DAX-1, and 11 beta-hydroxylase comparable to those in the transplanted intact adrenal gland.

CONCLUSIONS:

A tissue engineering approach that transplanted adrenal cortical cells seeded in a collagen scaffold was more effective than cell transplantation by direct injection. This methodology may be useful in the cell-based treatment of adrenal cortical insufficiency.

P42 DEVELOPMENT OF A MODEL SYSTEM FOR PRELIMINARY EVALUATION OF TISSUE ENGINEERED VASCULAR CONDUITS

<u>Amit Goyal</u>, Yinong Wang, Haili Su, Lawrence W. Dobrucki, Matthew Brennan, Peter Fong, Alan Dardik, George Tellides, Jordan Pober, W. Mark Saltzman, M.D., Ph.D., Christopher K. Breuer, M.D., Yale University, New Haven, CT, U.S.A.

PURPOSE:

The ability to construct neovessels with growth potential that could be used as arterial or venous grafts holds great promise for the advancement of pediatric surgical disciplines. While the feasibility of tissue engineering vascular grafts has been demonstrated, the long-term function, safety, and efficacy of these grafts remains largely unknown. In an attempt to further develop this technology we have sought to develop a small animal model that would allow rapid, cost effective, preliminary evaluation of tissue engineered vascular grafts.

METHODS:

To this end we have developed a SCID (severe combined immune deficiency) mouse vascular graft model. Eight SCID mice underwent vascular graft placement. Four mice under went aortic interposition grafting. One mouse underwent IVC interposition grafting, and three mice underwent aorto-caval graft insertion. All grafts were fashioned from decellularized ovine arteriole tissue engineering scaffolds. Grafts were evaluated for patency using clinical examination, ultrasound interrogation, and micro-CT.

RESULTS:

All grafts were patent based on clinical examination for up to 35 days. Patency was confirmed in five grafts using ultrasound interrogation. Patency was confirmed in four grafts using micro-CT. Animals were sacrificed at various time points after implantation and grafts were harvested and analyzed histologically using standard H&E staining. One animal that underwent AV grafting had to be euthanized secondary to high output cardiac failure on post-operative (POD) day 2. The remainder of the animals were sacrificed between POD 12 and 35. Histological evaluation of the specimen demonstrated patent grafts with cellular in-growth into the tissue engineering scaffold.

CONCLUSIONS:

From these results we conclude that the use of the SCID mouse model for preliminary evaluation of new tissue engineering methodologies for construction of vascular conduits is feasible. Use of this model has the added advantage of evaluating non-autologous and even xenograft tissue including human tissue.



Image 1: Mouse Aortic Interposition Graft

Underlining denotes the author scheduled to present at the meeting.

P43 GENE TRANSFER OF PIGMENT EPITHELIUM-DERIVED FACTOR SUPPRESSES TUMOR GROWTH AND ANGIOGENESIS IN EXPERIMENTAL HEPATOBLASTOMA <u>Marybeth Browne, M.D.</u>¹, Veronica Stellmach, Ph.D.², Mona Cornwell², Eun Jig Lee, M.D.², Lisa P. Abramson, M.D.¹, Riccardo A. Superina, M.D.¹, Marleta Reynolds, M.D.¹, Susan E. Crawford, M.D.², ¹Children's Memorial Hospital, Chicago, IL, U.S.A., ²Feinberg School of Medicine, Northwestern University, Chicago, IL, U.S.A.

PURPOSE:

Hepatoblastoma is the most common liver tumor in children and its growth is angiogenic dependent. Survival rate has improved with the advancement of chemotherapy and aggressive surgery; however, over 20% remain unresectable after initial treatment. PEDF is an endogenous anti-angiogenic factor known to be highly expressed in normal hepatocytes. We postulated that the loss of PEDF expression may be one mechanism driving hepatoblastoma growth and *in vivo* gene transfer of PEDF would suppress neovascularization and limit tumor growth.

METHODS:

Tumors were induced in athymic mice using subcutaneous injections of cultured human hepatoblastoma cells. One month after inoculation, tumors were injected with Ad-CMV-PEDF (n=4) or Ad-CMV-,gal (n=4) for 4 days. An additional 4 tumors served as controls. Animals were sacrificed at day 7, tumor weights were recorded, and tissue was stained with anti-PEDF, anti-factor VIII antibody, and Apotag. Mitotic figures, apoptotic cells, and microvascular density (MVD) were counted in 5 high-power fields (hpf).

RESULTS:

Ad-CMV-PEDF inhibited tumor growth compared to Ad-CMV-,gal (0.092g \pm 0.008 PEDF-Ad; 0.235g \pm 0.15 CMV-Ad). The amount of necrosis and number of apoptotic cells were increased in the Ad-CMV-PEDF treated animals. MVD and the number of mitotic figures were decreased in the Ad-CMV-PEDF group compared to the Ad-CMV-βgal and control groups.

CONCLUSIONS:

PEDF is an important endogenous regulator of the liver vasculature. Augmenting intratumoral PEDF levels inhibits tumor growth and angiogenesis in an experimental hepatoblastoma model. Potent inhibitors of angiogenesis, such as PEDF, may be an effective alternative treatment for children with unresectable or recurrent hepatoblastoma.

P44 GENERATION OF THE FIRST TRANSGENIC MOUSE EXPRESSING AN ENDOTHELIAL MARKER

Angela V. Kadenhe-Chiweshe, M.D., <u>Jae-O Bae, M.D.</u>, Paivi Ullner, M.D., Elizabeth Ferrari, B.S., Sulli Popilskis, D.V.M., Darrell Yamashiro, M.D., Jessica Kandel, M.D., Columbia University, New York, NY, U.S.A.

PURPOSE:

Recent studies support the importance of orthotopic cancer models which utilize human tumor cell lines, as these permit analysis of complex, multigenic events such as angiogenesis. However, these studies require xenografting in immunodeficient mice, which have proven difficult to use for transgenic studies. While perfusion techniques and immunohistochemical methods to analyze tumor vasculature are available, these do not unambiguously label all endothelial cell (EC) populations. We reasoned that nude mice engineered to express green fluorescent protein (GFP) on the Tie2 receptor, a marker for both precursor and mature EC, would demonstrate recruitment and organization of EC in xenografts.

METHODS:

All experiments were approved by the Animal Care Committee. Estrous cycles were induced in 3-week-old NCR nude female mice (nn, N=5) prior to mating with homozygous Tie2-GFP males (TT). On day 2.5 postcoitus, viable morulae were harvested, cultured 24h, then transferred as blastocysts day 3.5 to surrogate pseudo-pregnant mice. F1 heterozygotes (n=10; NnTt) were mated, and back-crossed for three generations to obtain TTnn offspring. Genotyping for Tie2GFP was performed by realtime PCR. Cultured human Wilms tumor SK-NEP-1 cells were then orthotopically implanted in nnTt/nnTT mice. Fixed-frozen sections of tumors and organs were used to analyze vasculature, using confocal microscopy and immunohistochemistry.

RESULTS:

GFP-labeled endothelium could be identified as individual cells, in capillary sprouts, and in mature vessels, using fluorescence microscopy. Complex three-dimensional vascular structures were analyzed by fluorescence confocal microscopy and specific immunohistochemistry for endothelial and vascular mural cells.

CONCLUSIONS:

We report the first immunodeficient mouse successfully engineered to express an endothelialspecific marker. These mice are fertile, viable, and support xenograft growth. Our study indicates that Tie2-GFP labeling permits the study of the origin and progression of EC involved in tumor angiogenesis, and may provide novel insights into the effects of anti-angiogenic agents in human tumors.

Scientific Session I: Diaphragmatic Hernia and Thoracic Diseases

 BIRTHWEIGHT AND MCGOON INDEX PREDICT SEVERITY IN NEWBORN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH) (6 MINUTES) <u>Germana Casaccia, M.D.</u>, F. Crescenzi, M.D., A. Dotta, M.D., I. Capolupo, M.D., A. Braguglia, M.D., O. Danhaive, M.D., L. Pasquini, M. Bevilacqua, M.D., Pietro Bagolan, M.D., M. Orzalesi, M.D., C. Corchia, M.D., Pediatric Hospital Bambino Gesù, Rome, Italy.

BACKGROUND:

Despite improvements in clinical management, mortality of CDH remains high. Early prediction of mortality risk helps in comparing strategies and/or performances of different centers. Birthweight (BW), Apgar score at 5' and McGoon Index (MGI) (the ratio between the size of pulmonary arteries and of descending aorta) have been utilized to determine severity of CDH.

PURPOSE:

To evaluate the relationship between early variables and survival in CDH infants intubated at birth, managed with "gentle" ventilation and delayed surgery.

METHODS:

34 CDH newborns, treated with a standardized protocol, were studied. MGI, BW, gestational age (GA), sex, side of CDH and prenatal diagnosis (PD) were recorded on admission. The relationship with mortality of each variable was evaluated by univariate analysis. Subsequentely, a predictive model of mortality was developed using a logistic regression: the explanatory variables, BW and MGI, were dichotomized in high (HBW and HMGI) and low (LBW and LMGI) according to the best cut-off found with ROC curves.

RESULTS:

The main characteristics of the 34 patients were (mean[range]): BW=2886[1500-3620]g; GA=37.7[32-42]wks; M/F=22/12; Right/Left=8/26; PD=29; MGI=1.31[0.9-1.85]. Only BW and MGI were significantly (p<0.05) associated with mortality at the univariate analysis. The best cut-off values were 2755 g for BW (sensitivity 70%, specificity 74%), and 1.25 for MGI (sensitivity 73%, specificity 78%). Using these limits, BW and MGI resulted independently associated with mortality in the multivariate analysis: ORs=7.2 (95%CI=1.1-47.8) for BW and 9.1 (95%CI=1.4-60.1) for MGI. Using the four possible combinations the predicted mortality rates were: HBW+HMGI=6%, HBW+LMGI=31%, LBW+HMGI=36%, LBW+LMGI=80%.

CONCLUSIONS:

BW and MGI, variously combined, were predictive of mortality. Since they are not influenced by subsequent modalities of care, they can be considered valid early severity scores in CDH and utilized for comparing strategies and/or performances of different centers.

2 PROSTHETIC PATCHES FOR CONGENITAL DIAPHRAGMATIC HERNIA REPAIR: SURGISIS® VERSUS GORE-TEX® (3 MINUTES)

<u>Erich J. Grethel, M.D.</u>, Raul A. Cortes, M.D., Amy J. Wagner, M.D., Matthew S. Clifton, M.D., Tiffany C. Townsend, M.D., Hanmin Lee, M.D., Diana L. Farmer, M.D., Michael R. Harrison, M.D., Roberta L. Keller, M.D., Kerilyn K. Nobuhara, M.D., University of California, San Francisco, CA, U.S.A.

PURPOSE:

The sequelae of congenital diaphragmatic hernia (CDH) continue well beyond the perinatal period. Studies have shown up to 50% of these patients have subsequent recurrence or small bowel obstruction. A recent trend has been toward the use of bioactive prosthetic materials which serve as a lattice for permanent tissue ingrowth. We retrospectively compared different patch closure techniques used for CDH repair at our institution.

METHODS:

Institutional approval was obtained by the Committee for Human Research. A retrospective review was performed of 160 records for patients with CDH treated at our institution. Patients undergoing patch repair for CDH and surviving for at least 30 days were included in the analysis. Outcomes evaluated were re-herniation and small bowel obstruction. Two types of prostheses were examined, Gore-tex[®] and Surgisis[®] (SIS).

RESULTS:

Thirteen out of 29 (45%) surviving patients who had a repair with SIS had a recurrence of the hernia. Two (7%) additional patients presented with small bowel obstruction. Seventeen out of 48 (35%) surviving patients who had repair with Gore-tex[®] had subsequent recurrence. Two (4%) additional patients presented with small bowel obstruction. Chi-squared analysis revealed a non-significant trend toward increased re-herniation and bowel obstruction in the SIS group (p = .46). The time course of the recurrences of both groups was similar (student's t-test, p = 0.94), with the majority of recurrences occurring in the first year.

CONCLUSIONS:

Despite advances in technology with the development of bioactive prosthetic materials, the rate of recurrence of congenital diaphragmatic hernia remained as high in a group of patients undergoing repair with SIS as it did in those undergoing repair with Gore-tex[®]. Patch failures may have been due to different etiologies in the two groups, and use of a composite mesh may be a viable alternative.

3 EFFECTS OF SURGICAL REPAIR OF CONGENITAL DIAPHRAGMATIC HERNIA (CDH) ON CEREBRAL HAEMODYNAMICS EVALUATED BY NEAR INFRARED SPECTROSCOPY (NIRS)* (3 MINUTES)

Andrea Dotta, M.D., Jole Rechichi, M.D., Francesca Campi, M.D., <u>Annabella Braguglia, M.D.</u>, Sabrina Palamides, M.D., Irma Capolupo, M.D., S. Lozzi, M.D., Alessandro Trucchi, Carlo Corchia, M.D., Pietro Bagolan, Marcello Orzalesi, M.D., Pediatric Hospital Bambino Gesù, Rome, Italy.

* The authors received a grant from the Italian Ministry of Health.

BACKGROUND:

Cardiorespiratory preoperative stabilization is recommended in CDH because surgery may induce a transitory deterioration of respiratory function. Changes in cerebral oxygenation are not still described during surgical intervention in CDH infants. Aim: To assess the effects of surgical repair of CDH, on cerebral hemodynamics. Subjects: 25 high risk CDH (BW 3057±353g; GA 37.8±1.8 wks, M/F 15/10, Left/Right CDH 19/6), ventilated by conventional "gentle" ventilation, stabilized and operated on at a median age of 2.7 dd (min-max: 2-14 dd).

METHODS:

Oxygen Saturation (SaO₂, %), Heart Rate (HR) and Mean Arterial Blood Pressure (MABP) were continuously monitored, FiO₂ adjusted to maintain preductal SaO₂ >80 %, while ventilator's settings were kept constant during surgery. Cerebral hemodynamics was assessed by NIRS, recording the changes in Oxygenated (Δ O₂Hb), Deoxygenated (Δ HHb) and Total (Δ CHb) Hemoglobin concentration and Tissue Oxygenation Index (TOI). CHb is considered an indirect index of cerebral blood volume (CBV).

RESULTS (expressed as means [range]):

At the beginning of surgery SaO2% was 95.0 [81/99] % with FiO₂ of 0.25 [0.21/0.40], TOI 70.0% [61/90], HR 148/m' [128/165] and MABP 54.0 cmH₂O [41/73]. At the end of surgery, FiO₂ increased to 0.35 (0.21/0.70; p<0.001) to maintain similar values of SaO2 (94.0 %; 83/100); nevertheless O₂Hb (p<0.001) and cHb (p<0.005) decreased and HHb (p<0.05) increased significantly (ΔO_2 Hb=-12.5 μ M [-25.8/+7.3]; Δ cHb= -10.2 μ M, [-26.2/+16.0]; Δ HHb=+3.8 μ M, [-10.4/+25.7]. HR increased significantly (166.0 b/m' [150/180]), while MABP did not change. The greatest changes occurred when the viscera were positioned into the abdomen.

CONCLUSIONS:

Surgical procedure is associated with a reduction in CBV and oxygenation. This is probably due to an increase in R/L shunt and a decrease in venous return. These results reinforce the recommendation that babies with CDH should be operated on when cardiorespiratory stabilization has been obtained.

Notes:

4 DIAPHRAGMATIC REPAIR THROUGH FETAL TISSUE ENGINEERING: A COMPARISON BETWEEN MESENCHYMAL AMNIOCYTE- AND MYOBLAST-BASED CONSTRUCTS (3 MINUTES)

<u>Shaun M. Kunisaki, M.D.</u>¹, Julie R. Fuchs, M.D.¹, Amir Kaviani, M.D.¹, Jung-Tak Oh, M.D.¹, David LeVan, Ph.D.², Joseph P. Vacanti, M.D.³, Jay M. Wilson, M.D.¹, Dario O. Fauza, M.D.¹, ¹Children's Hospital Boston, Boston, MA, U.S.A., ²Massachusetts Institute of Technology, Boston, MA, U.S.A., ³Massachusetts General Hospital, Boston, MA, U.S.A.

PURPOSE:

Engineered bioprostheses have been associated with low recurrence rates in a large animal model of diaphragmatic hernia repair. This study was aimed at comparing constructs seeded with mesenchymal amniocytes and fetal myoblasts and at determining the fate of these different cells *in vivo*, in this model.

METHODS:

Neonatal lambs (n=14) underwent repair of an experimental diaphragmatic defect with identical scaffolds, either seeded with labeled autologous cells (mesenchymal amniocytes in group I and fetal myoblasts in group II), or as an acellular graft (group III). At 1-12 months postoperatively, implants were harvested for analyses. Statistical comparisons were by the Fisher's exact and unpaired Student's t-tests, as appropriate (P<0.05).

RESULTS:

Repair failure was significantly higher in animals with acellular grafts (5/5, 100%) then in animals with engineered constructs (2/9, 22.2%), with no difference between groups I (1/4, 25%) and II (1/5, 20%). Labeled cells were found in all cellular grafts, however they lost their myogenic phenotype in group II, as evidenced by scant or negative desmin and skeletal myosin immunostainings. All groups contained cells with a fibroblastic-myofibroblastic profile. Vascular ingrowth by CD31 staining and overall cell density appeared enhanced in group I versus groups II and III. Both modular and ultimate tensile strengths were significantly higher in engineered than in acellular implants and significantly higher in group I (5.27 ± 1.98 and 1.94 ± 0.70 MPa, respectively) compared with group II (2.42 ± 0.97 and 0.45 ± 0.08 MPa, respectively). Elastin concentrations were significantly higher in group I ($81.81\pm16.81 \mu g/mg$) than in groups II ($65.02\pm25.70 \mu g/mg$) and III ($54.80\pm26.61 \mu g/mg$), with no differences in glycosaminoglycans and type-I collagen levels among the groups.

CONCLUSIONS:

Diaphragmatic repair with a mesenchymal amniocyte-based engineered tendon leads to improved structural and biomechanical outcomes when compared with equivalent fetal myoblast-based and acellular grafts. The amniotic fluid is a preferred cell source for engineered diaphragmatic reconstruction.

5 LUNG VOLUMES AND DISTRIBUTION OF VENTILATION DURING THE FIRST TWO YEARS OF LIFE IN INFANTS WITH CONGENITAL DIAPHRAGMATIC HERNIA (CDH)* (3 MINUTES)

<u>Andrea Dotta, M.D.</u>, Sabrina Palamides, Annabella Braguglia, Francesco Crescenzi, Germana Casaccia, Anna Maria Guadagni, Maria Paola Ronchetti, Pietro Bagolan, Carlo Corchia, Pediatric Hospital Bambino Gesù, Rome, Italy.

* The authors received a grant from the Italian Ministry of Health.

BACKGROUND:

CDH with lung hypoplasia is characterized by high morbidity and mortality during the neonatal period and by significant respiratory morbidity during infancy and childhood. "Gentle" ventilation and delayed surgery have been suggested to improve survival and long-term pulmonary sequelae; however the functional development during infancy has not been extensively studied so far.

PURPOSE:

To determine changes in lung function during the first two years of life in infants with CDH treated with a "gentle ventilation" and delayed surgery strategy during the neonatal period.

METHODS:

Thirteen CDH infants (means±SD: BW=3036±503g and GA=38.4±2.1wks, M/F=10/3, Left/Right CDH 11/2) were studied twice during the first two years of life, with at least six months between measurements. Tidal Volume (Vt), Respiratory Rate (RR) and time to peak expiratory flow/expiratory time ratio (tPTEF/Te, an index of lower airways patency) were measured with an ultrasonic flow-meter; Compliance (Crs) and Resistance (Rrs) of the respiratory system were studied with the single occlusion technique; Functional Residual Capacity (FRC) and Lung Clearance Index (LCI), a very sensitive and stable indicator of ventilation homogeneity, were assessed with sulphur hexafluoride (SF6) wash-in/wash-out technique. The differences between the first (T1) and second (T2) measurements were considered statistically significant for p <0.05 by the Student's t-test for paired values.

	Age at test (months)	Vt (ml/kg)	RR (a/min)	t-PTEF/Te	Crs (ml/cmH2O/kg)	Rrs (cmH2O/I/s)	FRC (ml/kg)	LCI
T1	4.5±2.5	8.1±1.9	49.2±12.9	0.21±0.08	2.1±0.4	52.2 ± 19.2	19.7±3.8	10.9±2.2
T2	11.9±4.2	9.5±1.7	31.5±6.0	0.18±0.05	2.3±0.6	53.0±25.8	20.3±4.7	12.2±3.1
р	-	<0.05	<0.01	n.s.	n.s.	n.s.	n.s.	n.s.

RESULTS:

The results are shown in the following table:

CONCLUSIONS:

Lung function in CDH survivors is characterized by a persistent impairment in lower airways patency as shown by high values of LCI (normal values < 7.5) and Rrs (normal values <40 cmH₂O/l/s). The severe ventilation inhomogeneity, even if the other lung function tests are within the normal range, can explain the high respiratory morbidity in older ages.
6 IS PERICOSTAL BAR FIXATION TECHNIQUE REALLY NECESSARY IN THE NUSS PROCEDURE?; SUBMUSCULAR BAR FIXATION TECHNIQUE (3 MINUTES) <u>Hyun Koo Kim, M.D., Ph.D.,</u> Young Ho Choi, M.D., Ph.D., Yang Hyun Cho, M.D., Se Min Ryu, M.D., Young-sang Sohn, M.D., Ph.D., Hark Jei Kim, M.D., Ph.D., Guro Hospital, Korea University Medical Center, Seoul, Republic of Korea.

PURPOSE:

Pericostal bar fixation technique is known to have low incidence of postoperative bar dislodgement in Nuss procedure, but due to the invasiveness of this procedure there is increased risk of complications. We evaluate the safety and stability of the less invasive bar fixation method which we performed.

METHODS:

This technique consists of placing both ends of the bar in the layer between the ribs and the serratus anterior muscle, and then fixing the bar into the submuscular pocket without pericostal bar fixation. One hundred thirteen patients who underwent Nuss procedure were divided into three groups according to bar fixation techniques. Group one consists of 25 patients who received bilateral pericostal bar fixation from August 1999 to August 2000. Thirty-nine patients in Group two received unilateral pericostal bar fixation from September 2000 to August 2001. And Group three, 49 patients received submuscular bar fixation without pericostal fixation from September 2001 to July 2004.

RESULTS:

Mean age at operation was 7.2 ± 5.67 years (range from 2 to 25 years) in Group one, 8.0 ± 5.53 years (range from two to 25 years) in Group two, and 8.8 ± 5.52 years (range from three to 24 years), respectively (p = NS). Bar dislodgement occurred in one patient (4%) in Group one, two patients (5.1%) in Group two, and one patient (2.0%) in Group three (p = NS). Hemothorax developed in two patients (8%) in Group one, two (5.1%) in Group two, and none (0%) in Group three (Group one vs. Group three, p < 0.05), and pneumothorax occurred in three patients (12%) in Group one, two patients (5.1%) in Group two, and two patients (4.1%) in Group three (p = NS).

CONCLUSIONS:

Submuscular bar fixation technique not only decreases technique-related complications but also has satisfactory results in preventing bar dislodgement at mid-term follow-up.

7 NON-OPERATIVE MANAGEMENT OF PECTUS CARINATUM (3 MINUTES) <u>Ala Stanford Frey. M.D.</u>, Greg Durrett, Certified Orthotist, Victor F. Garcia, M.D., Rebeccah L. Brown, M.D., Thomas H. Inge, M.D., Frederick C. Ryckman, M.D., Richard G. Azizkhan, M.D., Cincinnati Children's Hospital Medical Center, Cincinnati, OH, U.S.A.

PURPOSE:

The surgical correction of pectus carinatum entails subperichondrial resection of the prominent cartilages and transverse sternal osteotomy. However, the success of the Nuss Procedure prompted us to hypothesize that the non-invasive external application of sternal pressure may be effective in correcting pectus carinatum. Therefore, we reviewed our experience with the use of an orthotic custom fitted brace for the treatment of pectus carinatum.

METHODS:

We reviewed the charts of all children with a diagnosis of pectus carinatum from 1997-2004. Demographics, medical history, quality of life with and without treatment, activity limitations and complications were analyzed. Patients were managed with observation, operative repair, or an orthotic brace that provides continuous anterior and posterior sternal compression. The brace was to be worn 14-16 hours/day, for $2-2^{1/2}$ years, until vertical growth subsided.

RESULTS:

There were 101 patients, 80 male and 21 female; observation group (n=58), operative repair (n=18) and orthotic brace (n=25). Observation patients had mild deformities, with no intervention required at last visit. Uniformly, surgical patients had a positive outcome. Of the 25 children treated with a brace, 88% had complete resolution of their deformity. Patients with chest pain/pressure or shortness of breath with exertion were symptom free after correction. The mean follow up was two years. The earliest signs of correction were within three months of compliant brace wearing. Patients aged 12-14 had the best outcome. There were no complications of external bracing. Two non-compliant patients requested operative correction. Two patients have had insufficient follow-up. Compliance for the majority of children was high (89%) secondary to the hidden profile of the brace.

CONCLUSIONS:

The custom fitted brace is a safe and effective option for the repair of pectus carinatum. It should be offered as an early treatment alternative to children with a developing pectus carinatum in adolescence.

8 USE OF A BIODEGRADABLE PATCH FOR RECONSTRUCTION OF LARGE THORACIC CAGE DEFECTS IN GROWING CHILDREN (6 MINUTES) <u>Melvin D. Smith, M.D.</u>, Robert M. Campbell, University Texas Health Science Center, San Antonio, San Antonio, TX, U.S.A.

An extracellular matrix patch material, derived from porcine small intestinal submucosa (Surgisis: Cook, Bloomington, IN) has gained wide acceptance in the reconstruction of defects in various areas of the body. There are reports on its use in repair of inguinal and abdominal wall hernias, gynecologic and urologic areas, and adult thoracic wall and diaphragmatic support at the esophageal hiatus. There is very limited information in the literature on the use of Surgisis in the repair of thoracic cage defects in infants.

This paper concerns the efficacy of the biomaterial in reconstruction of the chest wall in 26 growing children since October 2001. These 26 children, part of a larger group of growing children, are undergoing thoracic cage reconstruction to correct anomalies of the ribs and spine that result in significant growth and pulmonary function restrictions. In conjunction with an expandable titanium prosthesis, the patch is used to gain a larger intrathoracic volume allowing lung expansion and growth. We feel that this work is the first of its kind to be reported.

At operation, the Surgisis patch is used when any one or more of the following conditions are present: a) herniation of lung is likely; b) chest wall musculature is significantly diminished; c) injury to the lung is likely at reoperation; d) the defect is over two by two centimeters.

During the followup period, three years thus far, Surgisis has not required removal for any reason. At reoperations, scheduled at six months intervals to lengthen the titanium prosthesis, the Surgisis is not encountered. The author of this report is the surgeon who has implanted all of the patches. The team feels that this material is excellently suited for use for the above conditions.

9 LONG-TERM FOLLOW-UP AFTER THYMECTOMY FOR MYASTHENIA GRAVIS: THORACOSCOPIC VS. OPEN (3 MINUTES)

<u>Amy J. Wagner, M.D.</u>, Raul A. Cortes, M.D., Erich J. Grethel, M.D., Matthew S. Clifton, M.D., Michael R. Harrison, M.D., Diana Farmer, M.D., Kerilyn K. Nobuhara, M.D., Jonathan Strober, M.D., Hanmin Lee, M.D., UCSF, San Francisco, CA, U.S.A.

PURPOSE:

To determine if children with myasthenia gravis are in remission or weaning off medication after thoracoscopic versus open thymectomy.

METHODS:

A retrospective review of patients who underwent thymectomy for myasthenia gravis at a tertiary referral center from 1992-2004 (n=14). IRB approval was obtained. Six patients (42.9%) underwent thoracoscopic resection. Eight patients underwent open resection; five had median sternotomy (35.7%) and three transcervical (21.4%) approaches. Follow-up was obtained in 12/14 (85.7%) of patients, by both chart review and by telephone. The median follow-up was 26.5 months (range= 4-111).

RESULTS:

The thoracoscopic group had a mean operating time of 138.8 minutes, compared to 139.8 in the open group (p=0.9). The thoracoscopic group had a mean estimated blood loss (EBL) of 7.5 ml compared to 52.5 ml in the open group (p=0.02). There were no complications in either group, and no patients required transfusion. The mean length of stay for the thoracoscopic group was 1.5 days (range= 1-2), and was 10.6 (range=3-41) in the open group (p=.13). Three of six (50%) patients were in remission in the thoracoscopic group at the time of follow-up. Similarly, 3/6 (50%) patients in the open group were in remission at follow-up. In the thoracoscopic group, 5/6 (83.3%) were in Class I-III of the DeFilippi Classification (remission or improved). One patient had no change in symptoms (Class IV). In the open group, 5/6 (83.3%) were classified as DeFilippi I-III at the time of follow-up. One patient experienced worsening symptoms (Class V).

CONCLUSIONS:

We conclude that there are similar results in both thoracoscopic and open thymectomy with over 83.3% of patients in both groups in remission or with improvement at the time of follow-up. Thoracoscopic thymectomy is an effective treatment for myasthenia gravis and is preferable to the open approach.

10 ESOPHAGEAL STRICTURES IN CHILDREN WITH EPIDERMOLYSIS BULLOSA: AN 11-YEAR EXPERIENCE WITH FLUOROSCOPY-GUIDED BALLOON DILATATION (3 MINUTES) Wolfageng Stohr M.D., Benjamin D., Hammolman, John M. Bacadia, M.D., Bichard C.

<u>Wolfgang Stehr, M.D.</u>, Benjamin D. Hammelman, John M. Racadio, M.D., Richard G. Azizkhan, M.D., Cincinnati Children's Hospital, Cincinnati, OH, U.S.A.

BACKGROUND:

Recessive dystrophic epidermolysis bullosa (RDEB) is an inherited mechanobullous disease affecting the skin and mucous membranes. Esophageal trauma caused by swallowing certain foods can lead to blistering, partial obstruction and ultimately esophageal strictures. These strictures lead to malnutrition and growth disturbances, significantly impairing the quality of life in children suffering from RDEB. In recent years initial management of esophageal strictures in these patients has evolved from bougienage and gastrostomy to endoscopically guided balloon dilatation. These techniques remain associated with a risk for oropharyngeal trauma caused by the endoscope. Our approach eliminates the need for endoscopy, thereby minimizing the risk for oropharyngeal trauma.

METHODS:

We conducted a review of all RDEB patients who underwent balloon dilatation for esophageal strictures between August 1993 and October 2004 at our children's hospital.

PROCEDURE:

Under general anesthesia an 8Fr feeding tube is introduced through the mouth into the esophagus. Under fluoroscopic control a flexible guide wire is inserted through the feeding tube into the stomach. The feeding tube is removed to allow insertion of a hydrostatic balloon catheter over the guide wire. The balloon is inflated with diluted water-soluble contrast and dilatation of the stricture is monitored fluoroscopically.

RESULTS:

Eighty four dilatations were performed on 24 patients ranging in age from two to 41 years. Between one and 14 procedures were performed on each patient. Dilatations were performed at intervals ranging from 1.5 months to 4.5 years. No significant complications were encountered, specifically no oropharyngeal blistering was observed postoperatively. All patients resumed their diet shortly after the procedure and could be discharged within 24h.

CONCLUSIONS:

Hydrostatic balloon dilatation under fluoroscopic guidance alone is a safe and effective treatment for esophageal strictures in RDEB patients. It minimizes oropharyngeal trauma and can be repeated as needed to maintain a good nutritional status and quality of life.

11 BRONCHIAL ATRESIA: THE HIDDEN PATHOLOGY WITHIN A SPECTRUM OF PRENATALLY DIAGNOSED LUNG MASSES (3 MINUTES) Shaun Kunisaki, M.D., Dario Fauza, Luanne Nemes, RNP, Carol Barnewolt, M.D., Judy Estroff, M.D., Harry Kozakewitch, M.D., <u>Russell Jennings, M.D.</u>, Children's Hospital Boston, Boston, MA, U.S.A.

PURPOSE:

Congenital lung masses have been commonly diagnosed prenatally. They are still typically divided in four distinct entities, namely congenital cystic adenomatoid malformation, bronchopulmonary sequestration, congenital lobar emphysema, and bronchogenic cysts. This study was aimed at determining whether these entities may actually be different manifestations of a single developmental abnormality associated with fetal airway obstruction.

METHODS:

A retrospective review of all infants (n=23) who had undergone surgical resection of a prenatally diagnosed lung mass over a three-year period was performed. In addition to standard examination by a pathologist, resected lesions were systematically assessed for the presence of bronchial atresia through painstaking full-specimen microdissections, as well as by both plain and contrast roentgenograms, as appropriate.

RESULTS:

Prenatal imaging sensitivity and specificity were respectively 100% and 65.2%, including missed mixed lesions in the latter index. Based on the final pathology reports, 15/23 (65.2%) cases were congenital cystic adenomatoid malfomations, 2/23 (8.7%) cases were congenital lobar emphysemas, 1/23 (4.4%) cases were bronchopulmonary sequestrations, and 5/23 (21.7%) cases had mixed cystic adenomatoid malformation and pulmonary sequestration features. No bronchogenic cysts were found in this series. Bronchial atresia was identified in association with all four different types of lung malformations, as well as with all five mixed lesions. Overall, 17/23 (73.9%) specimens were found to have a component of bronchial atresia. One specimen could not be completely evaluated because the surgical margin was felt to be distal to the segmental bronchi.

CONCLUSIONS:

Bronchial atresia is a common component of prenatally diagnosed congenital cystic adenomatoid malformations, bronchopulmonary sequestrations, and congenital lobar emphysemas. Most congenital lung masses may be part of a spectrum of anomalies linked to obstruction of the developing fetal airway as a common component of their pathogenesis.

12 PRENATAL DIAGNOSIS AND OUTCOME OF CHILDREN WITH PLEUROPULMONARY BLASTOMA (3 MINUTES)

<u>Douglas N. Miniati, M.D.</u>, Murali Chintagumpala, M.D., Claire Langston, M.D., Oluyinka O. Olutoye, M.D., Ph.D., Jed G. Nuchtern, M.D., Darrell L. Cass, M.D., Baylor College of Medicine, Houston, TX, U.S.A.

PURPOSE:

Pleuropulmonary blastoma (PPB) is a rare primary neoplasm of pleuropulmonary mesenchyme. Fewer than 100 patients have been reported, and few single institutions have reported more than several cases. Treatment for this condition is primarily surgical resection; however, increasing experience suggests that adjuvant chemotherapy may decrease recurrence and improve outcome.

METHODS:

We reviewed the charts of all children with PPB treated at our institution since 1960. We reviewed prenatal features, clinical presentation, operation, pathologic findings, adjuvant treatment and outcome.

RESULTS:

There were nine patients (five boys, four girls). In two a cystic lung mass was diagnosed prenatally on routine ultrasound, and in seven a cystic (n=4) or solid and cystic (n=3) lung mass was diagnosed postnatally (right lung- 3, left lung- 3, bilateral- 3). In no case was PPB considered preoperatively. All children had surgical resection at one day to 11 (median 1.6) years of age. Six patients had complete resection, one had microscopic residual disease, and two had gross residual disease. Pathology showed type I PPB in six, type II in two, and type III in one. Six patients received adjuvant chemotherapy with VAC-based regimens, and one patient was treated with radiation therapy. At follow-up (mean 46 months; range 2-167 months) six patients have no evidence of disease, one is alive with persistent disease, and two have died.

CONCLUSIONS:

Pleuropulmonary blastoma must be included in the differential diagnosis of a fetus or neonate with a cystic lung mass; and this supports the argument to resect these lesions rather than observe or treat with non-operative strategies.

Scientific Session II: Trauma and Hepatobiliary Diseases

13 DIAGNOSTIC AND THERAPEUTIC LAPAROSCOPY IN PEDIATRIC ABDOMINAL TRAUMA (6 MINUTES)

<u>Alexander Feliz, M.D.</u>, Barbara Shultz, R.N., B.S.N., Chris McKenna, CRNP, M.S.N., Barbara A. Gaines, M.D., Children's Hospital of Pittsburgh, Pittsburgh, PA, U.S.A.

PURPOSE:

The purpose of this study is to assess the role of emergent laparoscopy as a diagnostic and potentially therapeutic modality in pediatric trauma. We hypothesize that diagnostic laparoscopy provides important information for the treatment children with abdominal trauma and is accompanied by improved diagnostic accuracy, reduction of non-therapeutic laparotomy rates, shortened length of hospitalization, and a reduction of morbidity.

METHODS:

A five year (July 2000 to September 2004) retrospective review of a pediatric level I trauma center database was performed after IRB approval, and information regarding patients who had operations for abdominal trauma was abstracted. Demographic variables, mechanism of injury, operative interventions, and patient outcomes were examined. Statistical analysis was performed using descriptive statistics and student's t-test (p<0.05).

RESULTS:

There were 6,280 trauma admissions of which 107 had abdominal explorations for blunt (88%) and penetrating (12%) trauma. Thirty (28%) patients had laparoscopy performed. Laparatomy was avoided in 56.7% of these patients. Laparoscopic therapeutic interventions were performed in five (16.6%) patients. Laparoscopy assisted in the diagnosis and subsequent conventional repair of perforated viscera in nine patients, diaphragmatic rupture in three and distal pancreatic injury in one. Patients who had a laparoscopic procedure of any kind had a significantly lower number of ICU (0.7 ± 6.7 ; P<0.0006) and hospital days (7.3 ± 5.7 ; P<0.004) than patients who had a laparotomy (3.8 ± 7.3 and 12.7 ± 11.6). No injuries were missed, or technical complications occurred, as a result of laparoscopic explorations. There were five deaths in the laparotomy group. No patients who underwent laparoscopy died.

CONCLUSIONS:

Laparoscopy in pediatric trauma is a safe method for the evaluation and treatment of selective blunt and penetrating abdominal injuries in hemodynamically stable patients. Laparoscopy serves as a diagnostic tool in abdominal trauma which reduces the morbidity of a negative laparotomy. Improved diagnostic ability and minimally invasive interventions lead to shorter hospitalizations.

Notes:

14 ISOLATED CT DIAGNOSIS OF PULMONARY CONTUSION DOES NOT AFFECT MORBIDITY IN PEDIATRIC TRAUMA PATIENTS (3 MINUTES) Albert Kwon, <u>Donald L. Sorrells, Jr., M.D.</u>, John Cassese, M.D., Arlet G. Kurkchubasche, M.D., Thomas F. Tracy, Jr., M.D., Francois I. Luks, M.D., Ph.D., Brown Medical School, Providence, RI, U.S.A.

PURPOSE:

The diagnosis of pulmonary contusion has become more frequent with increasing sensitivity of CT imaging. The clinical significance of this finding has not been well defined. The purpose of this study was to examine the clinical course of patients with CT diagnosis of pulmonary contusion, and to correlate this with conventional radiographic findings.

METHODS:

The records of all consecutive pediatric trauma patients undergoing chest CT over a threeyear period were reviewed for age, mechanism of injury, Injury Severity Score (ISS), length of hospital stay (LOS), need for ICU admission and need for respiratory support including endotracheal intubation. A pediatric radiologist, blinded to the clinical findings and outcome, reviewed all CT scans and chest radiographs (CXR). Patients were divided into three groups: 1) Diagnosis of pulmonary contusion by CT only, 2) pulmonary contusion diagnosed by CXR, and 3) CT negative for pulmonary contusion. Statistical analysis (P<0.05 considered significant) was performed using ANOVA and Fisher exact test for 2 x 3 tables.

RESULTS:

There were no CXR-positive, CT-negative cases. Results are summarized in the table.

CONCLUSIONS:

Despite similar degrees of injury severity, children with pulmonary contusion by CT only have a much lower morbidity than children with pulmonary contusion evident on CXR. There was no difference in length of hospital stay, need for ICU or intubation between patients in the CT only and Control groups. The diagnosis of pulmonary contusion by CT scan, in the absence of CXR findings, does not appear to be a clinically relevant diagnosis warranting additional interventions.

CT vs. CXR diagnosis of pulmonary contusion							
	CXR positive CT only Control (CT negative) P						
N	31	15	38				
Age (yrs)	12 ± 5.5	14 ± 4.6	14 ± 4.7	NS			
ISS	27 ± 12.3*	22 ± 10.3*	15 ± 8.6	<0.01			
LOS (days)	13 ± 12	5 ± 3.6*	9 ± 9.5*	0.03			
ICU	28 (90%)	6 (40%)*	23 (61%)*	<0.01			
Intubated	20 (65%)	3 (20%)*	10 (26%)*	<0.01			

(*Difference between two groups not significant)

15 FACTORS INFLUENCING PEDIATRIC INJURY SEVERITY SCORE (ISS) AND GLASGOW COMA SCALE (GCS) IN PEDIATRIC AUTOMOBILE CRASHES: RESULTS FROM THE CRASH INJURY RESEARCH ENGINEERING NETWORK (CIREN) (3 MINUTES)

Peter F. Ehrlich, M.D.¹, <u>Joanna Brown, M.D.¹</u>, Mark Sochor, ¹, Stewart Wang, ¹, Martin R. Eichelberger, M.D.², 1University of Michigan, Ann Arbor, MI, U.S.A., ²Children's National Medical Center, Washington, DC, U.S.A.

PURPOSE:

Motor vehicle crashes(MVC) account for over 50% of pediatric injuries. Triage of pediatric patients to appropriate centers can be based on the crash/injury characteristics. Pediatric MVC crash/injury characteristics can be determined from an *in vitro* laboratory using child crash dummies. To date no detailed data with respect to outcomes and crash mechanism have been presented with a pediatric *in vivo* model.

METHODS:

CIREN is comprised of 10 level one pediatric trauma centers. Crashes were examined with regard to age, deceleration velocity at impact (ΔV), crash direction, restraint use and airbag deployment (AB). Multiple logistic regression analysis was performed with Injury Severity Score (ISS), and GCS as outcomes. Standard age groupings (0-4, 5-9, 10-14, 15-18) were used. The database is bias towards a survivor population with few fatalities. Analysis without fatalities did not impact results and fatalities are excluded.

RESULTS:

Four hundred and fifty MVC with 2,500 injuries were analyzed (240=males, 210=females). Irrespective of age $\Delta V > 30$ mph resulted in increased ISS and decreased GCS (e.g. 0-4yrs $\Delta V < 30$,ISS=10,GCS=13.5 vs. $\Delta V > 30$,ISS=19.5,GCS=10.6; p<0.007,<0.002 respectively). Controlling for ΔV , children in lateral crashes have increased ISS and decreased GCS vs. frontal crashes. *(Table one)* Belted children had lower ISS then unbelted children (ISS12.4vs17.6,p<0.01). Airbag deployment is protective for children 15 -18 results a lower ISS and higher GCS (OR2.1; CI 95% 0.9-4.6). Front seat passengers suffer more severe (ISS >15) injuries than back seat passengers (OR1.7, CI95% 0.7-3.4). A trend was noted for children under 12 sitting in the front sit to have increased ISS and GCS with AB deployment but was limited by case number.

CONCLUSIONS:

A reproducible pattern of increased ISS and lower GCS characterized by large impact, lateral crashes in children is noted. Further analysis of the specific injuries as a function the crash characteristic can help guide management and prevention strategies.

Direction of Crash Impact (controlled for ΔV) as function of ISS and GCS.(+/-SEM)							
Age	ISS			GCS			
	Frontal	Lateral	P value	Frontal	Lateral	P value	
0-4(N=96)	19.2±1.8	13.9±1.7	0.01	12.4±0.6	10.0±0.4	0.04	
5-9(N=49)	7.5±1.6	13.6±1.9	0.02	14.5±0.4	11.9±0.8	0.01	
10-14(N=82)	16.7±3.1	19.2±0.6	0.9	13.7±0.5	12.1±0.6	0.4	
15-18(n=44)	25.7±2.4	42.9±2.3	<0.01	12.1±0.6	6.5±0.8	<0.01	

16 DECOMPRESSIVE CRANIECTOMY IN PEDIATRIC TBI PATIENTS WITH REFRACTORY ELEVATED ICP (3 MINUTES)

<u>Daniel N. Rutigliano, D.O.</u>¹, Michael R. Egnor, M.D.², Jane E. McCormack, R.N.¹, Nancy A. Strong, R.N., CPNP², Richard J. Scriven, M.D.¹, Thomas K. Lee, M.D.¹, 1Department of Surgery, SUNY Stony Brook, Stony Brook, NY, U.S.A., ²Department of Neurosurgery, SUNY Stony Brook, Stony Brook, NY, U.S.A.

PURPOSE:

Care of pediatric traumatic brain injury (TBI) has placed emphasis on maximizing cerebral perfusion to prevent ischemia and reperfusion injury. A subset of TBI patients will continue to have refractory intracranial pressure (ICP) elevation despite aggressive therapy including ventriculostomy, pentobarbital coma, hypertonic saline, and diuretic. Decompressive craniectomy (DC) is a controversial treatment of severe TBI. It is our hypothesis that DC can enhance survival and minimize secondary brain injury in this patient subset.

METHODS:

Patients under age 20 year old treated at a Level I, Regional Trauma Center between 11/2001 and 11/2004, and who met inclusion criteria for the Brain Trauma Foundation TBI-tracTM clinical database were included. All patients with a mechanism of injury consistent with TBI and GCS of < 9 for at least six hours after resuscitation or GCS which deteriorated to < 9 within 24hrs and who did not die in the emergency department are entered into a clinical database. Functional Independence Measure (FIM) were recorded at the time of discharge. Patients are excluded who arrive to the study hospital more than 24 hours post injury.

RESULTS:

There were 30 TBI patients identified. The mean GCS at presentation was 8 with a range of 3-13. Six patients underwent DC for refractory elevated ICP. All patients recieved pre-op therapies according to the Brain Trauma Foundation protocol. Five of six post-op ICP were below 20. One patient required a follow-up cerebral debridement less than 24hrs post-op and subsequent ICP measurments were <20. All patients who underwent DC survived and were discharge to a TBI rehabilitation facility.

PT	Mechanism of Injury	1st ED GCS	HeadCT Midline shift/ Basal Cistern	Duration of ICP >20 Pre-DC	Hospital Length of Stay	GCS at Disch	FIM Ambulation	FIM Feeding
1	Ped struck	7	No /Open	26hrs	31 days	15	Assist	Assist
2	MVC	8	No /Part Open	18hrs	39 days	14	Assist	Independ
3	Ped struck	4	Yes /Part Open	2 hrs	19 days	12	Assist	Assist
4	Assault	3	Yes /Closed	3 hrs	24 days	14	Dependant	Dependant
5	Fall	13*	No/Open	5 hrs	18 days	14	Independ	Independ
6**	Bicycle	12*	No /Open	20 hrs	42 days	14	Assist	Independ

*Immediate deterioration to GCS<9

**Decompressive craniectomy, Debridement

(continued on next page)

CONCLUSIONS:

Although this is a small sample, decompressive craniectomy should be considered in TBI patients with refractory elevated ICP. Long-term follow-up of this patient population will consist of neuropsychiatric evaluation in conjuction with measurement of social functioning.

Notes:

17 THE IMPACT OF OBESITY ON SEVERELY INJURED CHILDREN AND ADOLESCENTS (3 MINUTES)

<u>Carlos V.R. Brown, M.D.</u>, Angela L. Neville, M.D., Ali Salim, M.D., Peter Rhee, M.D., MPH, Demetrios Demetriades, M.D., Ph.D., LAC/USC Medical Center, Los Angeles, CA, U.S.A.

PURPOSE:

In conjunction with the obesity epidemic in adults, we are starting to see an increase of obesity in children and adolescents. Obesity has been identified as risk factor for poor outcomes in adult trauma patients, but has not been investigated adequately in younger patients. The purpose of this study was to investigate the impact of obesity on the outcomes of a severely injured population of children and adolescents.

METHODS:

Retrospective review of traumatized children (age 6-12) and adolescents (age 13-19) admitted to the intensive care unit (ICU) at an urban, level I trauma center from 1998-2003. The trauma registry and ICU database were used for data acquisition. Height and weight were recorded for each patient upon admission to the ICU and used to calculate Body Mass Index (BMI). Patients were categorized as either lean (BMI < 30 kg/m²) or obese (BMI > 30 kg/m²). The two groups were compared regarding admission demographics, vital signs, mechanism of injury, patterns of injury, injury severity score (ISS), and operations required. Outcomes evaluated were need for and length of mechanical ventilation, complications, length of hospital and ICU stay, and mortality.

RESULTS:

There were 316 pediatric and adolescent trauma patients (273 [86%] lean, BMI = 23 kg/m² and 43 [14%] obese, BMI = 34 kg/m²) admitted to the ICU. The lean and obese groups were similar regarding age, gender, mechanism of injury, admission vitals, injury severity, and operations required. Injury patterns were similar, except obese patients suffered fewer head injuries (23% vs. 41%, p=.03). Outcomes in lean and obese patients shown below.

	Lean (n=273)	Obese (n=43)	p-value
Required ventilation	77% (211)	79% (n=34)	1
Days ventilated	3 + 5	5 + 8	0.04
Complications	23% (n=63)	40% (n=17)	0.04
Sepsis	4% (n=12)	16% (n=7)	0.005
ICU Stay (days)	6 + 6	9 + 9	0.04
Hospital Stay (days)	14 + 12	18 + 21	0.08

There was no difference in mortality between lean (14%) and obese (9%) patients (p=.48).

CONCLUSIONS:

Despite similar admission characteristics and fewer head injuries, obese children and adolescents suffer more complications and require longer mechanical ventilation and ICU stays than their lean counterparts.

18 OUTCOMES OF CHILDREN REQUIRING CPR FOLLOWING TRAUMATIC INJURY (3 MINUTES) <u>Kshama R. Jaiswal, M.D.</u>, Joceyln Chapman, B.S., R. Todd Maxson, M.D., Children's Medical Center Dallas and University of Texas Southwestern Medical Center, Dallas, TX, U.S.A.

PURPOSE:

The National Association of EMS Physicians and the American College of Surgeons Committee on Trauma issued guidelines for withholding or terminating resuscitation in adult traumatic cardiopulmonary arrest (TCPA) patients. However, there is a lack of data using TCPA pediatric populations. This study provides outcome data for the development of pediatric guidelines to withhold or terminate resuscitation after a TCPA.

METHODS:

A retrospective analysis of all patients at a level 1 pediatric trauma center who received pre-hospital CPR following a traumatic injury between January 1996 and June 2003 was performed. Injuries were categorized as penetrating or blunt. Age, gender, ethnicity, Glasgow coma scale (GCS), injury severity score (ISS), hospital charges, mechanism of injury (MOI), and outcome were examined.

RESULTS:

Sixty-six patients with a mean age of 5.9 ± 3.9 years were identified. Motor vehicle collisions (MVCs), auto/pedestrian collisions (MPCs), motorcycle collisions, falls, and "other causes" accounted for 58%, 19%, 3%, 3% and 16% of patients, respectively. Table 1 displays data points stratified as outcome. The overall survival rate was 9.1%. Blunt and penetrating trauma survival was 5% and 43%, respectively. Of all survivors, 50% suffered neurological deficiency. The positive predictive value (predicting a full recovery) for an ISS score less than or equal to one was 60% and the negative predictive value (predicting that a patient will not recover) for an ISS score greater than two was 100%. A closer look at the fully recovered survivors reveals cardiopulmonary arrest due primarily to anoxic insult.

CONCLUSIONS:

TCPA predicts a dismal outcome for pediatric patients. An ISS less than one, a history of asphyxiation, or penetrating trauma could predict successful resuscitation in TCPA patients. However, multi-center, prospective evaluation is warranted before guidelines for withholding or terminating resuscitation in pediatric patients can be supported.

Outcome	N	Age	M:F	MOI Blunt: Penetrating	ISS	Hospital Charges	Average Pt. Charges
Non- survivors	60	5.87	37:23	56:4	31.9 ± 17.4	\$1,178,520	\$19,642
Neurologically Deficient	3	3.75	1:2	2:1	23.7 ± 12.4	\$448,548	\$149,516
Fully Recovered	3	8.33	2:1	1:2	0.33 ± 0.22	\$328,037	\$109,346

Table 1. Outcomes After Traumatic Cardiopulmonary Arrest.

19 COMPARING TREATMENT OF PEDIATRIC SPLEEN INJURY AT TRAUMA CENTERS VERSUS NON-TRAUMA CENTERS: A CALL FOR DISSEMINATION OF APSA GUIDELINES (3 MINUTES)

<u>Steven Stylianos, M.D.</u>¹, Natalia Egorova, Ph.D., MPH¹, Karen S. Guice, M.D.², Ray Arons, DrPH¹, Keith T. Oldham, M.D.³, ¹Children's Hospital of New York, New York, NY, U.S.A., ²APSA Ctr for Outcomes, Milwaukee, WI, U.S.A., ³Children's Hospital of Wisconsin, Milwaukee, WI, U.S.A.

PURPOSE:

APSA consensus guidelines for children with blunt spleen injuries were defined and validated in children's hospitals (CH), however, large administrative data sets indicate that only 10-15% of children with blunt spleen injuries are treated at CH. We sought to identify the frequency and compare the treatment of children with spleen injury in hospitals with (TC) and without (Non-TC) trauma expertise.

METHODS:

State health department administrative data sets of California, Florida, New Jersey and New York were analyzed for 2000, 2001 and 2002. All children with head injury or other abdominal injuries requiring surgery were excluded. Trauma center designation was determined by the American Hospital Associations Directory, telephone inquiry and hospital web sites. Injury Severity Scores were determined by ICDMAP-90.

RESULTS:

Three thousand, two hundred eighty-five patients with blunt spleen injury were analyzed including 1,927 patients with isolated spleen injury. The latter group is summarized in the table below which includes the ICD-9 codes for blunt splenic injury severity. Adjusted odds ratio for risk of splenic operation in patients with isolated spleen injury was 2.122 (CI:1.455, 3.096) when treated at a non-TC versus a TC (p< 0.0001).

CONCLUSIONS:

These multi-state discharge data indicate that treatment of children with isolated blunt spleen injury differs significantly when comparing TC and Non-TC and that almost half (44%) of these children are treated at Non-TC. Better dissemination of APSA consensus guidelines and benchmarks to both TC and Non-TC may reduce the number of children receiving operation for isolated splenic injury.

	TC (n=1077)	Non-TC (n=850)	p value
Mean Injury Severity Score	8.6	9.2	NS
Overall Rate of Operative Treatment	9.23%	18.47%	< 0.0001
with hematoma (ICD-9: 865.01)	3.45%	3.92%	0.8
with capsular tear (ICD-9: 865.02)	4.76%	12.39%	< 0.02
with parenchymal laceration (ICD-9: 865.03)	12.17%	26.58%	< 0.004
with massive disruption (ICD-9: 865.04)	33.33%	46.67%	<0.02

Isolated Spleen Injury (n=1927)

20 OUTCOMES AND DELIVERY OF CARE IN PEDIATRIC TRAUMA (3 MINUTES) John C. Densmore, M.D., Keith T. Oldham, M.D., Karen S. Guice, M.D., Children's Hospital of Wisconsin, Milwaukee, WI, U.S.A.

PURPOSE:

In order to design trauma systems that meet the special needs of children, it is important to know where children currently receive trauma care and the outcomes of that care. Prior studies of pediatric trauma triage have been limited to single state and institutional experiences. Using a multistate administrative database, we describe recent allocation and outcomes in pediatric injury.

METHODS:

The KID 2000 database, containing 2,516,833 hospital discharge records from 27 states, was filtered by E-code to yield pediatric injury cases. These cases were then coded using ICDMAP-90, providing injury severity scores (ISS) in cases of urgent and emergent admission. Successfully mapped records were weighted to generate a national representation and resulted in 176,348 cases (poisoning, medical errors, adverse drug and late effects of injury excluded). Cases were grouped by age (0-10, >10-20 years), injury severity (ISS \leq 15, ISS > 15), and site of care (NACHRI designation). Measured outcomes included mortality, length of stay (<8d, \geq 8d) and total charges (<\$15K, \geq \$15K). Analysis was completed using t-test and Chi square.

RESULTS:

Among the 176,348 cases, mean age was 12.3 (SD=8.9) years and ISS was 7.0 (SD=10.9). 10% of children were patients in a children's hospital. Adult hospitals and children's units within adult hospitals cared for the remaining 67% and 23% respectively. The table below compares characteristics and outcomes of patients 0-10 years with an ISS > 15 in children's and adult hospitals.

	0-10 years, ISS >15 (n = 46,002)					
	Percent Cases	Mean ISS	Percent Mortality	Percent LOS ≥8d	Percent Charges ≥\$15K	
Childrens' General Hospital	26	18.9 (9.1)	5.3	45	36	
Adult General Hospital	35	19.4 (9.3)	7.6	45	35	
†t-test, * Chi sq		p=0.08†	p=0.002*	p=0.84*	p=0.26*	

CONCLUSIONS:

Thirty five percent of the youngest and most severely injured children received care at adult hospitals. Mortality rates for comparable injury severity were significantly higher in adult hospitals when compared to children's hospitals. There were no significant differences in length of stay or total charges between sites for this group. Increased triage of young and severely injured patients to children's hospitals may improve trauma related mortality.

Notes:

21 EFFECT OF CORTICOSTEROID THERAPY ON OUTCOMES IN BILIARY ATRESIA AFTER KASAI PORTOENTEROSTOMY (3 MINUTES)

<u>Mauricio A. Escobar, M.D.</u>, Colleen L. Jay, Ronald M. Brooks, Karen W. West, M.D., Frederick J. Rescorla, M.D., Jean P. Molleston, M.D., Jay L. Grosfeld, M.D., Indiana University, Indianapolis, IN, U.S.A.

PURPOSE:

This study tests the hypothesis that steroid administration improves the outcome of biliary atresia (BA) by evaluating the efficacy of postoperative steroid use on surgical outcomes in infants with BA.

METHODS:

Steroid use and outcomes in patients with BA were retrospectively analyzed at a tertiary pediatric hospital. IRB approval was obtained.

RESULTS:

Kasai portoenterostomy (PE) was performed in 43 patients with BA treated from 1992-2004 (16 boys: 27 girls). Twenty-one PE patients received steroids and 22 did not. PE was successful in 24 (55.8%) patients defined as a consistent serum bilirubin < 2 mg/dL. Sixteen (66%) received postoperative steroids. A normal postoperative bilirubin was achieved at six months in 16/21 (76%) patients with steroids compared to 8/22 (37%) in untreated controls (Fisher's exact test, p = 0.01). Nineteen of 43 (44%) required liver transplantation including 7/19 (37%) with steroids versus 12/19 (63%) without (p = 0.2). Twenty-eight infants developed cholangitis (fever with and without changes in hepatic function); 25 after PE and three after transplant. Eleven of 25 (44%) received steroids. Seven died (16%) (range seven mo-four yrs); two awaiting transplantation (received steroids) and five after transplantation (one received steroids, four untreated). Survival was 86% (18/21) in patients on steroids and 82% in those without (18/22). Transplant survival (74%) was comparable to previously reported historical controls (82%).

CONCLUSIONS:

The Kasai PE continues to be the procedure of choice in BA infants < three months of age. A significantly improved clearance of postoperative jaundice and lower serum bilirubin levels were observed in patients receiving steroids. However, steroids had no effect on the incidence of cholangitis, need for liver transplantation, and overall survival. A prospective study with standardized dose and length of steroid administration and longer period of follow-up is necessary to more accurately assess the effectiveness of steroids after PE.

22 RELIEF OF INTRACTABLE PRURITIS IN ALAGILLE SYNDROME BY PARTIAL EXTERNAL BILIARY DIVERSION (3 MINUTES) <u>Peter Mattei, M.D.¹, Daniel von Alllmen, M.D.², David Piccoli, M.D.¹, Elizabeth Rand, M.D.¹, ¹CHOP, Philadelphia, PA, U.S.A., ²UNC, Chapel Hill, NC, U.S.A.</u>

PURPOSE:

Alagille syndrome and other familial intrahepatic cholestasis syndromes can cause severe pruritis, hypertrophic skin changes, and xanthomatous skin lesions. In patients refractory to medical therapy, partial external biliary diversion is a treatment option for relief of these sometimes debilitating symptoms.

METHODS:

We present four patients with obstructive jaundice and severe intractable pruritis, three of whom underwent a partial external biliary diversion operation (cholecystojejunostomy) and one who had a cholecystostomy drain placed surgically.

RESULTS:

Three patients have a known diagnosis of Alagille syndrome. The fourth, an 11-month-old boy, has the diagnosis of progressive familial intrahepatic cholestasis (PFIC). Three patients, a 16-year-old girl, a 17-year-old boy, and an 11-month-old boy, underwent a partial external biliary diversion procedure using an isolated segment of jejunum as a conduit between the gallbladder and the skin. The bile drains into a standard ostomy appliance, which all three have managed without difficulty. All have had immediate and enduring relief of their pruritis. The older patients in the series also report significant improvement of the hypertrophic skin of their hands. In another patient, a 15-month-old boy with Alagille syndrome, external biliary drainage was achieved by placement of a cholecystostomy tube using an open surgical approach, which is changed periodically by an interventional radiologist. He has also had dramatic improvement of his symptoms and is being considered for formal partial biliary diversion. There was one complication, a reoperation after one week for bleeding from the primary jejunal anastomosis in the 11-month-old. Median follow-up is 10 months (range: 4 months to 22 months).

CONCLUSIONS:

Intrahepatic cholestasis syndromes such as Alagille syndrome can cause debilitating pruritis and deforming skin changes that are resistant to medical therapy. Immediate and lasting relief of pruritis and significant improvement in skin quality can be achieve by partial external biliary diversion.

Notes:

23 EFFECTIVENESS OF REX SHUNT IN THE TREATMENT OF PORTAL HYPERTENSION (3 MINUTES) <u>Roshini Dasgupta, M.D.¹, Eve Roberts, M.D.¹, Riccardo A. Superina, M.D.², Peter C. Kim¹, ¹Hospital for Sick Children, Toronto, ON, Canada, ²Children's Memorial Hospi</u>

*Kim*¹, ¹Hospital for Sick Children, Toronto, ON, Canada, ²Children's Memorial Hospital, Chicago, IL, U.S.A.

PURPOSE:

Children with portal vein thrombosis often have severe symptoms secondary to portal hypertension including recurrent UGI bleeds and hypersplenism. We report here the outcomes of the mesenterico-left portal vein bypass using internal jugular vein conduit (Rex Shunt) in five patients without evidence of liver dysfunction.

METHODS:

A retrospective chart review (REB# 1000001398) of all patients (n = 5) with portal vein thrombosis who underwent Rex Shunt procedure was done. MRA, doppler ultrasound and mesenteric angiogram were done to determine anatomic suitability for shunt procedure. Complete liver function and hematologic parameters were tested pre and post-operatively. Follow-up included doppler ultrasound in the immediate post-operative period and in clinic follow up.

RESULTS:

All patients had evidence of hypersplenism and 4/5 required recurrent transfusions and endoscopy and banding for serious UGI bleeds. The average age of the patients was 13.2 \pm 4.9 (7-19) years. The patient had an average of 2.6 \pm 1.7 UGI bleeds requiring banding, average 3.4 \pm 4.2 units of pRBC prior to undergoing the shunt. The mean operative time was 383 \pm 46 minutes and the mean length of stay was 10.4 \pm 7.1. One patient with a previous history of restrictive lung disease required prolonged ventilation in the post-operative period there were no further post-operative complications. Follow-up of mean of 13.8 \pm 5.2 months (mean of 6-19 months) all patients had patent shunts on Doppler ultrasound. No patients required any further endoscopic procedures or transfusions (p< 0.01), and no evidence of encephalopathy was noted. Splenic size did not decrease significantly on ultrasound however platelet counts normalized in patients that had been thrombocytopenic pre-operatively.

CONCLUSIONS:

The Rex shunt appears to re-establish normal portal blood flow. Shunt patency rate was 100% in this series. No recurrent variceal bleeds or evidence of encephalopathy was noted. The Rex shunt is effective in preventing variceal bleeds due to portal hypertension.

Scientific Session III: Gastrointestinal Tract

24 THE BIANCHI PROCEDURE: A 20-YEAR SINGLE INSTITUTION EXPERIENCE (6 MINUTES)

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PURPOSE:

The emergence of improved outcomes for small bowel (SB) transplantation has raised questions regarding the utility of autologous intestinal lengthening for patients with short bowel syndrome (SBS). Chronic immunosuppression, multiple hospitalizations and post-transplant lymphoproliferative disease are significant adverse factors. The purpose of this study is to evaluate the 20-year single institution experience with the Bianchi procedure and analyze its role in the management of pediatric SBS.

METHODS:

Medical records for 19 consecutive patients who underwent the Bianchi procedure from 1984 to 2004 were reviewed. Patients were categorized into three groups: < 5 years, $5 \le 9.9$ years and ≥ 10 years following surgery. Various outcome variables were evaluated as listed in Table 1. Data is presented in tabular format as the number of patients (%) or average (range).

RESULTS:

Nineteen patients were included in the study. Of 12 patients weaned from TPN, 4 (33%) responded to Bianchi procedure alone and eight patients (67%) required SB transplant at an average of 2.89 (0.7-8.13) years post-Bianchi. Four patients died (21%), One received SB transplant and died of unrelated causes, and three were still on TPN and had not received SB allograft.

CONCLUSIONS:

The Bianchi procedure facilitated weaning from TPN and eliminated the need for supplemental nutrition in select patients. Although the role of surgery is primarily adjunctive in the

treatment of SBS, it offers therapeutic benefit in decreasing parental nutrition requirements and promoting intestinal adaptation. In particular, the Bianchi procedure has significant potential to improve the prognosis of pediatric patients with SBS.

Parameter	Time Since Bianchi Procedure				
Tarametti	Result (% OR range)				
	< 5 years	$5 \le 9.9$ years	> 10 years		
		(%)	(%)		
Number of patients	6	7	6		
Gender					
Male	3 (50)	4 (57)	5 (83)		
Female	3 (50)	3 (43)	1 (17)		
Diagnosis					
Midgut Volvulus/Intestinal Ischemia	1 (17)	1 (14)	3 (50)		
Jejunal Atresia/Small Bowel Atresia	2 (33)	3 (43)	2 (33)		
Gastroschisis	3 (50)	3 (43)	1 (17)		
Average					
Weight Percent	6.83 (1-15)	5.71(1-12)	2.17 (1-6)		
Height Percent	4.67 (1-15)	3.00 (1-7)	1.00 (all)		
Gestational Age (weeks)	35.33 (33-40)	35.71 (32-40)	38.00 (36-40)		
Age at Time of Bianchi (yrs)	1.36 (0.17-6.25)	0.99 (0.42-2.17)	2.63 (1.25-4.00)		
Small Bowel Length At Diagnosis (cm)	32.17 (13-50)	27.64 (9-42.5)	36.80 (18.3-78)		
Percent Small Bowel Remaining (%)	13.87 (5-25)	11.10 (6.5-21)	12.88 (7-26)		
Time Since Bianchi (yrs)	3.15 (1.75-4.25)	6.68 (5.42-8.33)	13.56 (10.92-19.92)		
Small Bowel Transplant	3 (50)	4 (57)	2 (33)		
Number of patients on TPN	6 (100)	7 (100)	3 (50)		
Successful Wean from TPN	4 (67)	5 (71)	3 (50) *		
Death	1 (17)	3(43)	0		

* Weaned off TPN prior to small bowel transplant

25 THE ROLE OF LAPAROTOMY FOR INTESTINAL PERFORATION IN VERY LOW BIRTH WEIGHT INFANTS (6 MINUTES)

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PURPOSE:

The management of intestinal perforation in very low birth weight (VLBW) infants (<1500g) is controversial. Current practice favours peritoneal drainage (PD) with or without a secondary laparotomy (SL) over primary laparotomy (PL). We compared the outcomes of PD+/-SL versus PL in VLBW infants using the Score for Neonatal Acute Physiology with Perinatal Extension (SNAPPE-II) as a validated predictor of mortality.

METHODS:

With IRB approval, a retrospective analysis (1995-2003) of VLBW infants with intestinal perforation at two pediatric centres was undertaken. Data retrieval included neonatal demographics and parameters for SNAPPE-II calculation. The primary endpoint was 30-day mortality. Other outcome measures included fasting (NPO) days, days to extubation and length of stay (LOS). Statistical analysis was performed using the Fisher exact test or ANOVA. Subgroup and multivariate analyses were performed. P-values < 0.05 were considered significant.

RESULTS:

Fifty-two neonates (25PD:27PL) were reviewed. Overall, 10 infants died (19.2%). Observed 30-day mortality rates in PD and PL groups were 32% and 7.4% (p=.028), respectively. Average SNAPPE-II scores for PD (42.5 ± 20.8) and PL (25.1 ± 14.6) groups yielded predicted mortality rates of 15.7% and 4.9% (p=0.001), respectively. PD group 30-day mortality far exceeded the predicted rate. NPO days (13.7 vs. 20.4; p=0.0001), days to extubation (26.7 vs. 51.5; p=0.014) and LOS (56.1 vs. 83.6; p=0.031) all favoured the PL group despite incorporating SNAPPE-II score as a covariate into the multivariate analysis. Of the 25 patients receiving drainage, nine underwent PD alone (SNAPPE-II=46.6 \pm 27.9) while 16 patients underwent SL (SNAPPE-II=37.8 \pm 17.6). The PD only group had a greatly elevated mortality rate (77.8% vs. predicted 15.7%) while the PD+SL group had a reduced mortality rate (6.3% vs. predicted 9.3%).

CONCLUSIONS:

Our data suggests laparotomy either alone or after peritoneal drainage is the preferred treatment option in VLBW infants with intestinal perforation. Peritoneal drainage should be used as a temporizing measure until laparotomy can be performed.

26 LAPAROSOPIC NISSEN FUNDOPLICATION WITHOUT DIVISION OF SHORT GASTRIC VESSELS IN CHILDREN: IS "MORE FLOPPY" OVERRATED? (3 MINUTES) <u>Marco V. Melis, M.D.</u>, Mindy B. Statter, M.D., Loretto Glynn, M.D., Tony Lin, M.D., Donald C. Liu, M.D., Ph.D., University of Chicago, Chicago, IL, U.S.A.

PURPOSE:

It has been suggested that routine division of the short gastric vessels (SGV) results in a more "floppy" Nissen fundoplication leading to improved outcomes, i.e., less dysphagia and lower incidence of recurrent gastroesophageal reflux disease (GERD). The aim of this retrospective study was to assess whether laparoscopic Nissen fundoplication (LNF) without division of SGV (Rossetti-modification) is associated with acceptable clinical outcome.

METHODS:

The charts of 368 children with medically-refractory GERD who underwent LNF without division of SGV between January 1996 and September 2004 by one primary surgeon were retrospectively reviewed. Three hundred twelve children (84.8%) were either severely neuro-logically impaired or delayed. Children were divided into two groups for purposes of assessing surgical outcome: LNF + gastrostomy (A); LNF alone (B). Mean follow-up of all groups was 3.7 years (range: 1-93 mos.).

RESULTS:

LNF was completed in 365/368 (99%). Mean operating time for (A) = 74 min. (range: 36-180 min.); (B) = 61 min. (range: 31-120 min.). No children in (A) required post-operative esophageal dilatation; nine children in (B) (22.5%) required 12 dilatations (range: 1-3) for persistent dysphagia/gas bloat. Four children (B) required subsequent temporary gastrostomy, three of whom had mild to moderate neurological impairment. Thirteen of 365 (3.6%) developed recurred GERD during a mean follow-up of 3.7 years; 12 (3.7%) in (A) and one (2.5%) in (B).

CONCLUSIONS:

Laparoscopic Nissen fundoplication without division of short gastric vessels can be performed with acceptable long term outcome in all children with severe GERD, especially in the majority requiring simultaneous gastrostomy for feeding issues related to neurological impairment. Short term, reversible dysphagia may be seen in a small percentage of children having fundoplication alone and may be minimized by better selection criteria.

27 NEW CLINICAL AND THERAPEUTIC PERSPECTIVES IN CURRARINO SYNDROME (STUDIES OF 28 CASES) (6 MINUTES) <u>Claire Nihoul Fékété</u>, Celia Crétolle, Stanislas Lyonnet, Francis Jaubert, Sabine Sarnacki, Hopital des Enfants Malades, Paris, France.

PURPOSE:

Our purpose was to better define the anomalies, which compose the Currarino syndrome. We insist on the frequency of associated malformations of the spinal cord and the possibility of a communication between the presacral tumor and the spinal canal, leading to neurological complications. We applied a single-stage surgery technique with combined neurosurgical and digestive approach. In parallel, we are exploring the genetic events leading to this well-defined syndrome of caudal regression.

METHODS:

We studied 28 Currarino patients including eleven familial cases. The sacral, hindgut and neurological anomalies were precisely characterized and histological analysis of the malformative presacral tumor was performed. Cytogenetic and molecular biology studies of the *HLXB9* locus were carried out.

RESULTS:

All patients but one had a sacral malformation; 22 had an anorectal malformation and 24 had Chronic Intestinal Pseudo Obstruction. Twenty presacral tumors were diagnosed at a mean age of five years; these were a teratoma in nine cases, a meningocele in six cases and combined benign tissues in five; there was a communication between the tumor and the spinal canal in 12 cases, and a tethered spinal cord in 18 cases. Twenty-one patients were operated, 10 with a single-stage surgery on both intestinal and presacral tumor malformations. Twelve of 28 patients harbored a heterozygous point mutation of the coding sequence of *HLXB9* gene.

CONCLUSIONS:

Currarino syndrome is a clinical entity that should be evoked in the presence of combined sacral and hindgut anomalies. A spinal MRI should always be performed in search of the presacral tumor and the medullary anomaly. A posterior perineal surgical approach allows simultaneous treatment of intestinal and neurological malformations. Molecular biology may lead to early diagnosis in familial cases, and ultimately allows better understanding of the embryological underpinnings of this anomaly.

28 THE ROLE OF PROLIFERATION AND APOPTOSIS IN THE PATHOGENESIS OF INTESTINAL ATRESIA (6 MINUTES)

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PURPOSE:

Intestinal atresia occurs in 1:5,000 live births, offering a neonatal surgical challenge. Embryologic expression of Fibroblast growth factor 10 (*Fgf10*), acting through Fibroblast growth factor receptor 2b (*Fgfr2b*), has been shown to be critical to normal intestinal development. Invalidation of the *Fgf10* pathway results in several intestinal atresia phenotypes inherited in an autosomal recessive pattern. Previous studies show the *Fgf10^{-/-}* and *Fgfr2b^{-/-}* colonic atresia animal model does not result from a mesenteric vascular accident as classically understood. The purpose of this study was to determine the role of proliferation and apoptosis in the pathogenesis of intestinal atresia.

METHODS:

Wild type (Wt), *Fgf10^{-/-}* and *Fgfr2b^{-/-}* embryos were harvested from timed pregnant mice. The gastrointestinal tract was dissected, preserved and sectioned with standard techniques. Slides were treated with TUNEL (Terminal deoxynucleotidyl Transferase Biotin-dUTP Nick End Labeling) and BrdU (bromodeoxyuridine) immunohistochemistry protocols. Photomicrographs of the embryonic Wt and mutant intestine were compared at key developmental time points. Animals were utilized under IACUC approved protocol 32-02.

RESULTS:

Photomicrographs of Wt and mutant intestine shown at early stages of embryonic development demonstrate that invalidation of the *Fgf10* pathway results in an inhibition of proliferation and an increase in apoptosis. The inhibition of proliferation and increased apoptosis are specific to those tissues where *Fgf10* is normally expressed and where atresia occurs.

CONCLUSIONS:

The absence of embryonic enteral expression of *Fgf10* or its receptor *Fgfr2b* results in intestinal atresia in mice. FGF10 acting on its receptor FGFR2B is required for the proliferation of embryonic intestinal cells. In the absence of this signaling cascade, intestinal cells are preprogrammed to enter an apoptotic cellular pathway which results in intestinal atresia. The inhibition of proliferation and up-regulation of apoptosis of intestinal cells as a cause of intestinal atresia represents a novel concept in the pathogenesis of intestinal atresia.

(graphic on next page)



29 OUTCOMES OF ROUX EN Y GASTRIC BYPASS IN ADOLESCENTS: A MULTICENTER REPORT FROM THE PEDIATRIC BARIATRIC STUDY GROUP* (6 MINUTES) Louise Lawson, Ph.D.¹, Shelley Kirk, Ph.D., R.D.¹, Stephen Daniels, M.D., Ph.D.¹, Carroll M. (Mac) Harmon, M.D., Ph.D.², <u>Mike Chen, M.D.³</u>, Victor Garcia, M.D.¹, Thomas Inge, M.D., Ph.D.¹, ¹Cincinnati Children's Hospital Medical Center, Cincinnati, OH, U.S.A., ²Children's Hospital of Alabama, Birmingham, AL, U.S.A., ³University of Florida, Gainesville, FL, U.S.A.

* Dr. Harmon is a consultant for Stryker Endoscopy.

PURPOSE:

Our aim is to describe one year weight loss and CV risk profile results of adolescent Roux-en-Y gastric bypass surgery in patients \leq 21 years of age.

METHODS:

We conducted a retrospective chart review of adolescents undergoing surgery at three centers. The primary outcome measure was weight change at one year (data available for n=31). Secondary outcomes were complications (n=41) and mean changes in features of metabolic syndrome (n=10-24). Data were analyzed using sign rank or paired t-tests.

RESULTS:

Initial mean body mass index (BMI) fell 30% from 55.7 to 35.6 kg/m² at 1 year postoperative (p<0.001). In a comparable cohort (n=12) in medical weight management BMI fell 2.6% (47.2 to 46 kg/m² p=NS). Surgical patients had significant decreases in triglycerides (-65 mg/dL, p<.01), total cholesterol (-28 mg/dL, p<.001), fasting blood glucose (-12 mg/dL, p<0.02) and fasting insulin (-21 IU/uL, p<.001). Changes in HDL cholesterol (-3.9 mg/dL) and LDL cholesterol (-8.7 mg/dL) were not significant. Of 41 patients with \ge one year of postoperative observation, 24 (63%) had no complications. Of 15 with complications, nine had minor complications with no long term sequelae (including wound infection, stricture, and dehydration), 4 had \ge 1 moderate complication with sequelae for \ge 1 month (including nutritional deficiencies leading to anemia or neuropathy, and staple line leak) and 2 had \ge 1 severe complication with long term (>30 days) consequences (including beriberi and death). There were no perioperative deaths.

CONCLUSIONS:

Adolescent bariatric patients experience significant weight loss and improvements in features of the metabolic syndrome. The complication profile is similar to adults, some of which can be attributed to difficulties in adherence with the post-operative nutritional regimen. Adolescent bariatric patients should be monitored closely by a multidisciplinary team to detect and optimally manage surgical and medical complications.

30 ATYPICAL MALROTATION: IS OBSERVATION SAFE? (3 MINUTES) <u>Christine M. Habib, M.D.</u>, Richard J. Jackson, M.D., Evan R. Kokoska, M.D., Samuel D. Smith, M.D., Arkansas Children's Hospital, Little Rock, AR, U.S.A.

PURPOSE:

Atypical malrotation is an increasingly common diagnosis on upper gastrointestinal (UGI) contrast studies. Prior review of malrotation at our institution revealed a lower risk of volvulus and internal hernia with higher morbidity of operation in atypical malrotation as compared to classic malrotation. The purpose of this study is to determine if observation alone is a safe alternative in the management of atypical malrotation.

METHODS:

Patient records with radiographic diagnosis of malrotation from February 2000-October 2004 were reviewed. Atypical malrotation was defined anatomically by the ligament of Treitz located at or to the left of midline and/or below the gastric outlet at the level of the 12th thoracic vertebra on UGI contrast study. Patients with atypical malrotation treated operatively were compared with those observed.

RESULTS:

Of 174 total patients, a preoperative radiographic diagnosis of classic malrotation was present in 76 patients and that of atypical malrotation in 98. All patients diagnosed with classic malrotation were treated with Ladd's procedure. Based on presenting symptoms, 66 patients (67%) with atypical malrotation underwent Ladd's procedure with a 9% postoperative complication rate. Twenty nine (30%) exhibited only gastroesophageal reflux symptoms and were observed with repeat UGI contrast study in four weeks. Eight patients (8/29 or 28%) subsequently required operation based on colicky abdominal pain, bilious emesis, and/or feeding intolerance. Two of these patients (7%) had postoperative complications. Twenty one atypical malrotation patients initially observed (21/29 or 72%) remain asymptomatic. Four patients in the observation group had repeat UGI studies interpreted as normal, avoiding further intervention. No patients in the atypical malrotation group managed nonoperatively developed volvulus or internal hernia during observation.

CONCLUSIONS:

Observation is a safe treatment option in the management of atypical malrotation patients who are asymptomatic or exhibit gastroesophageal reflux symptoms only.

31 HB-EGF DECREASES THE INCIDENCE OF NECROTIZING ENTEROCOLITS IN NEONATAL RATS (6 MINUTES) <u>Jiexiong Feng, M.D., Ph.D.</u>, Osama N. El-Assal, M.D., Ph.D., Gail E. Besner, M.D., Children's Hospital, Columbus, OH, U.S.A.

PURPOSE:

The aim of this study was to determine the effect of enterally administered HB-EGF on the incidence of necrotizing enterocolitis (NEC) in neonatal rats.

METHODS:

NEC was induced in neonatal rats delivered via C-section (day 21 gestation) by hypertonic formula feeding coupled with hypoxia and hypothermia (HTFHH) plus enteral administration of LPS (2 mg/kg). Sixty-two neonatal rats were randomly divided into four groups. Group 1 pups (n=10) were breast-fed. Group 2 pups (n=10) received hypertonic formula without other stress. Group 3 pups (n=20) were subjected to HTFHH+LPS. Group 4 pups (n=22) were subjected to HTFHH+LPS with HB-EGF (600 lg/kg) supplementation in the formula. Animals were monitored until 96h of life for clinical signs of NEC. Intestines were collected and the presence and severity of NEC were evaluated using a standard histologic scoring system. The incidence and severity of NEC between groups were analyzed with x2 analysis and Mann-Whitney test, respectively. The survival time was analyzed by Kaplan-Meier analysis. For all analyses, p<0.05 was considered significant.

RESULTS:

The incidence of NEC in group 3 was higher than that in group 1 or 2 (65% vs 0% and 10% respectively, both p values less than 0.01). With administration of HB-EGF, the incidence (27.3% in group 4 vs. 65% in group 3, p<0.05) and severity (median injury score 1.1 in group 4 vs. 2.0 in group 3, p<0.05) of NEC were decreased significantly. Administration of HB-EGF also increased survival rate (63.6% in group 4 vs. 25% in group 3, p<0.05) and survival time (75h in group 4 vs. 60h in group 3, p<0.05).

CONCLUSIONS:

We conclude that HB-EGF reduces the incidence and severity of NEC in a neonatal rat model. These results support our contention that HB-EGF administration may represent a useful therapeutic and prophylactic strategy for the treatment of NEC.

32 HEPATOCYTE GROWTH FACTOR (HGF) INCREASES GLUCAGON IMMUNOREACTIVITY IN JEJUNAL CELLS DURING INTESTINAL ADAPTATION (3 MINUTES)

<u>Shaheen J. Timmapuri, M.D.</u>¹, David M. Otterburn, M.D.¹, Hwyda Arafat, M.D., Ph.D.¹, Marshall Z. Schwartz, M.D.², ¹Thomas Jefferson University, Philadelphia, PA, U.S.A., ²Thomas Jefferson University, St. Christopher's Hospital for Children, Philadelphia, PA, U.S.A.

PURPOSE:

The administration of HGF during intestinal adaptation is known to enhance intestinal adaptation. Glucagon has also been implicated as a potential mediator of intestinal adaptation. Previous studies have shown that HGF and glucagon synergistically increase the proliferation of hepatocytes. HGF has also been shown to be preferentially expressed within the glucagon positive cells of the pancreas, possibly indicating a paracrine or endocrine effect of HGF on glucagon. This study was designed to determine if HGF stimulation in the small intestine during intestinal adaptation influenced mucosal glucagon expression.

METHODS:

Adult male Sprague-Dawley rats were randomized to either a 70% massive small bowel resection group (MSBR) or an HGF treated MSBR group (MSBR-HGF). Seven days after surgery, HGF was administered intravenously at 150ug/kg/day for 14 days. At day 21, ileal and jejunal mucosa was harvested. The RAE 230A GeneChip and MAS5 software were used to determine alterations in gene expression in the small intestine mucosa. Immunofluorescent staining of the ileal and jejunal mucosa using an anti-glucagon antibody was performed and evaluated qualitatively.

RESULTS:

The MSBR-HGF group had significantly greater protein and DNA content (p< 0.05) than the MSBR group. However, glucagon gene expression in the MSBR-HGF group was decreased compared with the MSBR group. Immunohistostaining for glucagon in the ileum revealed no difference in intensity between the two groups. However, the jejunal MSBR-HGF group demonstrated significantly greater glucagon immunoreactivity than the jejunal MSBR group.

CONCLUSIONS:

Our data suggests that the HGF-induced increase in glucagon availability is disassociated from glucagon gene up-regulation. Thus, HGF may not only enhance intestinal adaptation directly, but also indirectly by increasing the "local" availability of other growth factors in the absence of their gene up-regulation.

33 USE OF A BAYESIAN NETWORK IMPROVES THE ACCURACY OF PHYSICIANS DIAGNOSING INFANTS WITH SUSPECTED PYLORIC STENOSIS (3 MINUTES) <u>Sonia M. Alvarez, M.D.</u>, Beverly A. Poelstra, M.D., Randall S. Burd, M.D., Ph.D., UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.

PURPOSE:

Up to 75% of infants undergoing an ultrasound to rule out pyloric stenosis will have a negative study, suggesting the low accuracy of clinical assessment. Bayesian networks are decision tools that use probabilistic relationships among features of a disease to improve diagnostic accuracy. The purpose of this study was to evaluate the feasibility of using a Bayesian network to improve the accuracy of diagnosing pyloric stenosis.

METHODS:

Records of 118 infants undergoing an ultrasound to rule out pyloric stenosis were reviewed. Data from 88 infants (75%) were used to train a Bayesian network that used risk factors, signs and symptoms to predict the probability of pyloric stenosis (training set). The emergency room records of the remaining 28 infants (25%) were used to test the network (testing set). Two panels of pediatric surgeons and pediatric emergency medicine physicians were asked to predict the probability of pyloric stenosis in the testing set: 1) physicians using the network and 2) physicians using only emergency room records. Accuracy was evaluated using the area under the ROC curve (ROC) [discrimination] and the Hosmer-Lemeshow (H-L) c-statistic [calibration].

RESULTS:

Pyloric stenosis was found in 51/88 (58%) of infants in the training set and 17/28 (61%) in the testing set. Physicians using the Bayesian network more accurately predicted the probability of pyloric stenosis among infants in the testing set than those not using the network (ROC 0.973 vs. 0.882; H-L c-statistic 3.9 [p>0.05] vs. 24.3 [p<0.05]). Physicians using the network missed no cases of pyloric stenosis (negative predictive value 100%, 95% CI 87%-100%) and would have ordered 22% fewer ultrasounds.

CONCLUSIONS:

A Bayesian network improves the accuracy of physicians diagnosing infants with possible pyloric stenosis. Application of this decision tool may safely reduce the need for diagnostic imaging among infants with suspected pyloric stenosis.

34 VALUE OF SURGERY IN DIRECTING THERAPY OF WILMS TUMOR PATIENTS WITH PULMONARY DISEASE. A REPORT FROM NATIONAL WILMS TUMOR STUDY (NWTS) — 5 (6 MINUTES)

Peter F. Ehrlich, M.D.², <u>Tom E. Hamilton, M.D.¹</u>, Robert C. Shamberger, M.D.³, Michael Ritchey, M.D.⁴, Gerald Haase, M.D.⁵, Paul Grundy⁶, ¹Main Medical Center, Portland, ME, U.S.A., ²University of Michigan, Ann Arbor, MI, U.S.A., ³Harvard University, Boston, MA, U.S.A., ⁴University of Texas, Houston, TX, U.S.A., ⁵Denver Children's Hospital, Denver, CO, U.S.A., ⁶Alberta Children's Hospital, Edmonton, AB, Canada.

PURPOSE:

Computerized tomography (CT) of the chest with its increased sensitivity frequently identifies lesions not visible on chest radiograph. Treatment such for lesions is controversial. A recent review suggests that patients with lesions detected by CT only treated with dactinomycin and vincristine have an inferior outcome compared to those who received pulmonary radiation therapy (RT) and doxorubicin (DOX) as well. It is important to determine if these small lesions represent disease and whether such pts with CT only disease require RT and/or DOX for optimal outcome while minimizing toxicity.

METHODS:

WT patients with lung metastases registered on NWTS-5 and for whom a radiology and surgical checklist were submitted with CT only lesions were reviewed. The treatment regimens of these patients and histologic findings of the pulmonary lesions are presented. We analyzed patients by single vs. multiple lesions.

RESULTS:

Two thousand, four hundred ninety-eight patients were registered on NWTS-5 with 252 of these patients with pulmonary metastases. Of these patients, 129 (5.2%) had CT only lesions. Forty-two of these patients (20 boys and 22 girls) underwent lung biopsy at the discretion of the attending physicians. The treatment stage in these patients was Stage I-n=3 (two drugs); II-n=3 (two drugs); III-n=12 (three drugs); and IV-n=24 (three drugs+RT). There were 16 patients with isolated lung lesions and 26 with multiple lesions, average size 5.8 ± 0.5 mm. Thirteen of 16 isolated lesions (82%) and 18/26 patients (69%) with multiple lesions had tumor on biopsy. Eight of the 24 who received RT had a negative biopsy thus may not have needed the RT. Five of six treated with just two drugs may have been under treated. Nine of 12 treated with three drugs had tumor on biopsy.

CONCLUSIONS:

CT only lesions are not invariably tumor, demonstrating the need for histopathologic confirmation. Biopsy remains critical until radiographic techniques allow differentiation between benign and malignant lesions.

35 PRIMARY HEPATIC METASTASES IN NEPHROBLASTOMA — A REPORT OF THE SIOP/GPOH STUDY (6 MINUTES) <u>Philipp O. Szavay, M.D.¹, Norbert Graf, M.D., Ph.D.², Tobias Luithle, M.D.¹, Rhoikos Furtwängler², Joerg Fuchs, M.D., Ph.D.¹, ¹University of Tuebingen, Tuebingen, Germany, ²University of Homburg/Saar, Homburg, Germany.</u>

PURPOSE:

Remarkable progress could be achieved in the treatment of nephroblastoma within the last decades. In all children with a Wilms' tumor five-year overall survival rate reaches 91.79% in the SIOP/GPOH study group. Despite this fact there is a small group of patients who has tumor lesions in the liver primarily representing a challenge in treatment. The data of this group should be analyzed.

METHODS:

In order to define survival and success of treatment of this group of patients we reviewed the records of 29 out of 1,365 patients enrolled in the SIOP 93-01/GPOH Study and the SIOP 2001/GPOH Study between April 1st, 1994 and September 30th, 2004.

RESULTS:

Median age at diagnosis was 10.61 years (0.19-34.16 years). All patients but two underwent nephrectomy. Liver metastases were operated in 11 children at time of nephrectomy, while in 14 patients liver lesions were treated by chemotherapy alone. In two children no treatment could be initiated. Fifteen patients received radiotherapy additionally. Eleven patients died in the course at a median of 13.07 months (0.25-42 months) after initial diagnosis. These included seven patients who never had surgery for their liver lesions, and four patients who had incomplete and/or atypical resections of their metastatic liver lesions. Those patients who underwent complete resection of hepatic metastases (n = 6), survived. Eight children survived with a non-surgical treatment. Overall survival was below 60% in the whole group up to now.

CONCLUSIONS:

Liver metastases are much less frequent than metastases to other sites. Our report suggests that Wilms' tumor complicated by metastases of the liver primarily has a less favorable outcome. High dose chemotherapy and radiotherapy have a role in treatment but also for palliation in metastatic disease. Radical surgery for nephrectomy as well as for surgery of liver lesions cannot be overemphasized in order to prevent local and distant recurrence.

36 TUMOR INHIBITION CORRESPONDS TO PERTURBATION AND RECOVERY OF VASCULATURE DURING SUSTAINED POTENT VEGF BLOCKADE (3 MINUTES) <u>Angela V. Kadenhe-Chiweshe, M.D.</u>, Jason Frischer, M.D., Jae-O Bae, M.D., Jianzhong Huang, M.D., Jessica Kandel, M.D., Darrell Yamashiro, M.D., Columbia University, New York, NY, U.S.A.

PURPOSE:

Vascular endothelial growth factor (VEGF) blockade has recently been validated in clinical trials involving treatment-refractory adult tumors. Metastatic, unresectable hepatoblastoma (HBL) is an example of a childhood cancer refractory to current regimens. Previous work suggests that established tumors may be regressed by VEGF inhibition, but may recur during long-term blockade. Tumor vessel recovery may be supported by mural cell (VMC) recruitment, a process stimulated by multiple factors, including platelet-derived growth factor-B (PDGF-B) and angiopoietin-1 (Ang-1). We hypothesized that experimental HBL would exhibit VMC recruitment and vascular recovery during sustained VEGF blockade.

METHODS:

All experiments were approved by the Animal Care Committee. HBL tumors were established by injecting 10(6) cultured human HBL-HUH6 cells intrarenally in NCR nude mice, and allowing tumor growth for 6wk. A randomly-selected initial cohort were sacrificed (N=10, day 0), and remaining mice randomly assigned to treatment and control groups, receiving soluble decoy receptor construct (VEGF-Trap) or vehicle biweekly, respectively. Tumors were harvested and analyzed at intervals until day 44.

RESULTS:

VEGF blockade arrested growth in late-stage HBL (day 44, 6.9 \pm 1.0g, control, vs. 2.0 \pm 0.3g, treated, P<0.02). Treated tumors displayed initial (day 15) collapse of vasculature, loss of differentiated VMC, and widespread necrosis. By day 44, tumors displayed vessel recovery, with (1) VMC recruitment (2) increased PDGF-B and Ang-1expression (3) increased concurrent enhanced anti-apoptotic signaling in endothelium. Endothelium in recurrent tumors expressed phosphorylated-Akt, a key mediator of phosphotidylinositol-3-kinase survival signaling. Day 44 tumors were again proliferative, with reorganization of viable cells in perivascular trabeculae.

CONCLUSIONS:

Progressive vascular recovery, characterized by recruitment of VMC and anti-apoptotic signaling, may rescue HBL tumors that are initially destabilized by VEGF blockade. Factors modulating vascular cell survival appear to participate in this program of response, and may provide novel targets to enhance anti-angiogenic therapeutic strategies.

37 STUDY OF THE FACTORS ASSOCIATED WITH RECURRENCE IN CHILDREN WITH SACROCOCCYGEAL TERATOMA (3 MINUTES)

<u>Toon De Backer, M.D.</u>, Gerard Madern, M.D., Friederike Hakvoort, M.D., Frans W.J. Hazebroek, M.D., Ph.D., Academic Hospital, Free University of Brussels, Brussels, Belgium and Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands.

PURPOSE:

To explore effects of (1) histologic involvement of resection margins, (2) incomplete coccyx removal, (3) tumor spillage on recurrence in children operated upon for sacrococcygeal teratoma (SCT).

METHODS:

Retrospective review of 70 SCT patients treated between 1960 and 2003.

RESULTS:

Fifty-four patients were female, 16 male. 36% of tumors were Altman type I, 27% II, 18% III and 18% IV. Histologically, 48 patients had mature teratoma (MT), 11 immature teratoma (IT), nine yolk sac tumor (YST), one embryonal carcinoma, one mixed tumor. Eighty-four percent of patients, solely underwent surgical extirpation. Six patients died (8.5%). Mortality in patients treated during the past 15 years had dropped to 2.5%. Tumor recurrence was observed in five patients, two of whom died. Of three patients with initially MT, one showed local immature recurrence and two malignant distant recurrences (YST). One of the latter died. Of two patients with initially IT grade I, one showed relapse as a benign lesion and one YST recurrence leading to death. All patients but one had possible eliciting factors. Histologic analysis of resection margins showed tumoral involvement in 12 patients. Only one of those, with YST focus in the resection margin, showed recurrence. Intraoperative tumor spillage presented in two patients, who both died from metastatic disease. Spillage of tumoral cyst fluid occurred in six, none developed recurrence. One of five patients whose coccyx had not been removed died from metastatic disese. One with IT developed a benign recurrent tumor. The other three showed no recurrence.

CONCLUSIONS:

Microscopic involvement of the resection margins of (im)mature SCT is rarely associated with recurrence, provided there are no YST foci in the resection margins. A conservative attitude then appears to be justified. Spillage of cyst fluid was never associated with recurrence, whereas spillage of tumor and absence of removal of coccyx frequently was.

38 LIVER TRANSPLANTATION FOR CHILDHOOD HEPATIC MALIGNANCY: IS IT A VIABLE OPTION? (3 MINUTES) <u>Mary T. Austin, M.D.</u>, Charles M. Leys, M.D., Irene D. Feurer, M.D., Harold N. Loworn, M.D.,

James A. O'Neill, M.D., C. Wright Pinson, M.D., M.B.A., John B. Pietsch, M.D., Vanderbilt University Medical Center, Nashville, TN, U.S.A.

BACKGROUND:

Liver transplantation (LT) is the only treatment option for unresectable hepatoblastoma (HB) and hepatocellular carcinoma (HCC) in children. Outcomes of LT for these hepatic malignancies have not been evaluated in the UNOS national database.

PURPOSE:

To evaluate patient survival in pediatric LT recipients with HB and HCC and identify factors that differentiate these diagnoses.

METHODS:

Data from the UNOS Standard Transplant and Research Files were analyzed and included pediatric (< 18 years) LT recipients with HB or HCC from 1987 to 2004. The effects of diagnosis on pre-transplant variables were evaluated using t-tests or Chi-square analyses, as appropriate. Actuarial survival and effect of diagnosis on survival were determined using Kaplan-Meier methods and log-rank tests.

RESULTS:

Since 1987, 152 LTs have been performed in 135 patients for HB and 43 LTs in 41 patients for HCC. Respective one-, five- and 10-year patient survival following LT was 79%, 69%, and 66% for HB and 86%, 63% and 58% for HCC (p=0.73). The primary cause of death for both groups was metastatic or recurrent disease, accounting for 54% deaths in the HB group and 86% in the HCC group (p=0.338). HB patients were younger (p<0.0001) and more likely to receive a living donor organ (16% vs. 4%, p=0.03). A greater proportion of the HB patients had previous abdominal surgery than HCC patients (63% HB vs. 37% HCC; p=0.04). Pre-transplant medical condition and transplant era were associated with survival on univariate analysis (p=0.002 and p=0.015, respectively). Only transplant era was independently associated with survival in the multivariate model (p=0.04).

CONCLUSIONS:

LT remains a viable option for pediatric patients with unresectable primary hepatic malignancies and results in good long-term survival. Most patient deaths are secondary to recurrent disease. With improved patient selection and better chemotherapy regimens, LT may result in further improved long-term survival.

39 SURVIVAL AFTER LIVER TRANPLANTATION FOR HEPATOBLASTOMA: A TWO CENTER EXPERIENCE (3 MINUTES)

<u>Marybeth Browne, M.D.</u>¹, Dani Sher, B.A.¹, Lisa P. Abramson, M.D.¹, David Grant, M.D.², Enza Deluca, R.N.², Estella Alonso, M.D.¹, Peter F. Whitington, M.D.¹, Riccardo A. Superina, M.D.¹, ¹Children's Memorial Hospital, Chicago, IL, U.S.A., ²Hospital for Sick Children, Toronto, ON, Canada.

PURPOSE:

Complete resection with adjuvant chemotherapy is the accepted treatment for hepatoblastoma. The aim of this study was to evaluate our results of orthotopic liver transplantation (OLT) for tumors still unresectable after adequate chemotherapy.

METHODS:

All patients transplanted for hepatoblastoma from two institutions between 1990 and 2004 were included. Variables reviewed to determine impact on survival included: OLT done as primary surgery or secondarily for recurrent tumor after previous resection, metastatic disease at diagnosis, histological vascular invasion, alpha fetoprotein levels at diagnosis and at transplant, tumor histology, and administration of post-transplant chemotherapy. Effectiveness of pre-transplant chemotherapy was defined as a drop of more than 99% in peak AFP levels.

RESULTS:

There were 14 patients transplanted: nine boys and five girls (age range 18 months-13 years, mean age 57 \pm 48 months). Patients were transplanted a mean of 4 \pm 1 months after diagnosis. Overall survival was 71% (10/14) with a mean follow-up of 46 months. All deaths were secondary to recurrent tumor. Nine of 10 patients who underwent a primary OLT survived compared to only one of four with recurrent tumor after major prior resection (90% vs. 25%, p=0.02). Decline in peak AFP of more than 99% was also associated with better survival (100% vs. 56%, p = 0.08). Similarly, patients who received post-transplant chemotherapy had 100% survival compared to 56% without chemotherapy (p=0.08). Other variables had little effect on survival (see table).

Variables		# of Patients	Survival	p value
Primary transplant	yes	10 (71%)	9 (90%)	0.02
	no	4 (29%)	1 (25%)	
Post-transplant chemotherapy	yes	5 (36%)	5 (100%)	0.08
	no	9 (64%)	5 (56%)	
AFP at transplant < 1% of peak AFP	yes	5 (36%)	5 (100%)	0.08
	no	9 (64%)	5 (56%)	
Pulmonary metastasis at diagnosis	yes	2 (14%)	1 (50%)	0.4
	no	12 (86%)	9 (75%)	
Histological vascular invasion	yes	8 (57%)	6 (75%)	0.7
	no	6 (43%)	4 (67%)	
Histology of tumor	mixed	10 (71%)	6 (60%)	0.3
	embryonal	2 (14%)	2 (100%)	
	fetal	2 (14%)	2 (100%)	
CONCLUSIONS:

OLT for hepatoblastoma when done as a primary procedure has significantly better survival than transplantation for recurrent disease. Patients with good pre-transplant control of AFP or those who were given chemotherapy after transplantation also had improved survival, but the differences only approached significance. Multi-center collaboration to validate these findings with a larger patient population is necessary.

40 CLINICAL PRESENTATION, TREATMENT, AND OUTCOME OF ALVEOLAR SOFT PART SARCOMA IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS (3 MINUTES) Mark L. Kayton, M.D., Paul Meyers, M.D., Leonard H. Wexler, M.D., <u>Michael P.</u> <u>LaQuaglia, M.D.</u>, Memorial Sloan-Kettering Cancer Center, New York, NY, U.S.A.

PURPOSE:

Alveolar soft part sarcoma is a rare soft tissue neoplasm that can affect children and adolescents, resulting from an (x, 17) translocation. There are few reported series of these patients in the literature. To define the clinical presentation, treatment, and outcome of young people with this rare sarcoma we reviewed our clinical experience.

METHODS:

Following IRB approval, we examined the records of 13 patients under age 25 who received treatment at our institution for alveolar soft part sarcoma since 1984. Demographic data, sites of disease, treatments employed, condition at last followup, and survival were evaluated.

RESULTS:

Median age at diagnosis was 17 years (range 6-24). All patients presented with a mass. Primary disease sites included extremities (n=6), head and neck (n=2), chest/breast (n=4), and psoas (n=1). Lung metastases were present in seven, and among these two had brain metastases as well. Six patients had disease amenable to wide local excision . Three patients underwent pulmonary metastasectomy, from one to eight times. Of the nine patients who underwent wide local excision +/- metastasectomy, eight remained free of disease with a median disease-free followup of 13.5 months (range: 1-173). Four non-surgical candidates had progression of disease on combinations of chemotherapy, radiation, and investigational agents. Notably, four patients presented to us with incomplete excision of the primary (positive margins) and one underwent embolization of what was mistakenly thought to be an AVM.

CONCLUSIONS:

These data support the use of wide local excision for primary site control of this neoplasm. In addition, metastasectomy may provide long-term disease free survival in selected patients with pulmonary dissemination, the most common site of metastases. A surprising proportion of patients presented to us with incompletely resected primary tumors, suggesting a need for greater use of needle or incisional biopsies to establish the diagnosis prior to local excision.

41 OPEN THORACOTOMY IS THE BEST THERAPY FOR METASTATIC OSTEOGENIC SARCOMA (3 MINUTES)

<u>Mark L. Kayton, M.D.</u>, Jennifer Casher, B.A., Sara J. Abramson, M.D., Nancy S. Rosen, M.D., Leonard H. Wexler, M.D., Paul Meyers, M.D., Michael P. LaQuaglia, M.D., Memorial Sloan-Kettering Cancer Center, New York, NY, U.S.A.

PURPOSE:

Survival in osteogenic sarcoma correlates with complete resection of primary and metastatic disease. The feasibility of complete pulmonary metastasectomy using thoracoscopy has been raised. Since palpation is not possible, minimally invasive techniques require pre-operative radiologic enumeration and localization of metastases not presenting at the lung surface. We hypothesized that CT scanning underestimated the number of pulmonary metastases in these patients.

METHODS:

IRB approval was obtained. We determined the association between the number of lesions identified by CT scanning and the number of metastases found at thoracotomy for metastatic osteogenic sarcoma at our institution from May 9, 1996 to Oct. 8, 2004. Two pediatric radiologists, blinded to the outcome of each thoracotomy, determined by consensus the number of nodules on preoperative CT. The number of metastases resected was determined from operative notes and pathology reports. Patients with miliary disease (>25 nodules) were excluded. Correlation was computed using the Kendall-tau-b correlation coefficient (similar to the R² in linear correlation).

RESULTS:

We analyzed 54 consecutive thoracotomies performed in 28 patients for whom complete imaging was available. Scanning was performed a median of 20 days prior to thoracotomy (range: 1-85 days). Correlation between number of lesions identified by CT and number of metastases resected at surgery is depicted in Figure 1. Kendall-tau-b correlation coefficient was 0.53. In 13 thoracotomies (24%), CT scanning underestimated the number of metastases identified at thoracotomy.

CONCLUSIONS:

Even in the era of modern CT scanning, only a very rough correlation exists between CT findings and the number of lesions identified at thoracotomy. In 24 percent of thoracotomies in our series, metastases would have been missed by any tactic besides manual palpation of the lung during open thoracotomy. Until more sensitive imaging is available, minimal access procedures should not be the approach of choice if the goal is resection of all pulmonary metastases.

(graphic on next page)

Figure 1



Notes:

Underlining denotes the author scheduled to present at the meeting.

42 LONG-TERM SURVIVAL AFTER AGGRESSIVE RESECTION OF PULMONARY METASTASES AMONG PATIENTS WITH OSTEOSARCOMA (3 MINUTES) <u>Matthew T. Harting, M.D.¹, Martin L. Blakely, M.D.², Norman Jaffe, M.D., D.Sc.³, Charles S. Cox, Jr, M.D.¹, Andrea Hayes-Jordan, M.D.¹, Robert S. Benjamin, M.D.³, Richard J. Andrassy, M.D.¹, Kevin P. Lally, M.D.¹, ¹University of Texas Medical School at Houston, Houston, TX, U.S.A., ²University of Tennessee Health Science Center, Memphis, TN, U.S.A., ³MD Anderson Cancer Center, Houston, TX, U.S.A.</u>

PURPOSE:

An aggressive approach is recommended for osteosarcoma patients with pulmonary metastases. Although survival without resection is unlikely, long-term follow-up after aggressive resection is uncommon and demographic or tumor characteristics likely to favor long-term survival are virtually unknown.

METHODS:

A single institution retrospective cohort study of osteosarcoma patients <21 years of age with pulmonary metastases, limited to the contemporary chemotherapeutic time period (1980-2000), was completed.

RESULTS:

Radiographically evident pulmonary nodules were identified in 137 patients either at presentation (23.4%) or subsequently (76.6%). Median follow-up was 2.5 years (five days to 20.1 years) for all patients and 5.4 years (1.0 year to 19.7 years) for 25 survivors. Overall survival (OS) at three and five years was 40.2% and 22.6%, respectively. Ninety-nine patients had attempted lung metastases resection (mean survival=33.6 months; 95% CI, 25.1-42.1); 38 patients did not (mean survival=10.1 months; 95% CI, 6.5-13.6; p<0.001, t-test). Characteristics that were associated with an increased likelihood for 5-year OS were primary tumor necrosis after neoadjuvant chemotherapy >98% (p=0.046, chi-square) and diseasefree interval (DFI) prior to developing lung metastases (diagnosis until detection of metastases) >one year (p<0.001, chi-square). No difference in OS or disease-free survival was found based on the number of pulmonary metastases resected. Other characteristics including primary tumor size, site, or extension, chemotherapy, timing of metastases, unilateral vs. bilateral metastases, complete resection vs. incomplete, pleural disruption, resection margins, and necrosis of metastases did not significantly affect survival.

CONCLUSIONS:

The majority of patient characteristics commonly used by surgeons to determine the aggressiveness of resection of pulmonary metastases among patients with osteosarcoma were not associated with outcome. Characteristics likely related to the biology of a particular tumor (response to preoperative chemotherapy, measured by tumor necrosis percentage, and DFI) appear to be highly associated with patient outcome. Aggressive resection should be attempted to prolong survival.

43 C-MYC INHIBITION NEGATIVELY IMPACTS LYMPHOMA GROWTH (6 MINUTES) <u>R. Serene Perkins, M.D.</u>, Stephen P. Dunn, M.D., Ilsa Gomez-Curet, Ph.D., Katherine L. Feidler, B.S., Leslie J. Krueger, Ph.D, AI duPont Hospital for Children, Wilmington, DE, U.S.A.

PURPOSE:

Epstein-Barr Virus (EBV) associated and EBV independent lymphomas are linked to C-MYC deregulation. Different genetic mechanisms of deregulation include translocation, amplification, and somatic mutation. This diversity underscores the universal significance of C-MYC deregulation during lymphomagenesis. For these reasons C-MYC is actively being targeted as a potential therapeutic candidate.

METHODS:

Hu95A microarrays (Affymetrix, Santa Clara) were used to investigate genes deregulated in an EBV-associated B-cell line, TIB-215. A time course of global profiling was obtained at 0-time, 9, 12, 15, 18, 21, 24, and at 40 hrs of synchronously dividing cultures. This approach evaluated approximately 12,000 tiled probe sets using high-density oligomer chips. Results of altered gene expression were subsequently confirmed by MGB-TaqMan real time PCR. (*Z*,*E*)-5-(4-Ethylbenzylidine) -2-thioxothiazolidin-4-one (EMD Biosciences, San Diego), a C-MYC inhibitor was used to inhibit cell growth. Specificity was determined using knockout (-/-), parental and transfected C-MYC cells. Experiments were done in a series of EBV-associated LCL and BLs with 8-replicates per experimental point (24 hr intervals) over a three-day period.

RESULTS:

The initial demonstration of C-MYC deregulation was obtained by microarray analysis. This was subsequently confirmed by quantifying mRNA levels using TOPO-cloned C-MYC by MGB-TaqMan real time PCR. By targeting C-MYC with a direct inhibitor, TIB-215 proliferation was significantly inhibited at each time point within a time frame of 72 hrs. The antiproliferative effect of C-MYC inhibition was common to all LCL and BL cell lines tested. This inhibitor works by blocking the formation of the nuclear MYC-MAX heterodimer and therefore, did not effect significant changes in C-MYC mRNA.

CONCLUSIONS:

By targeting C-MYC, the proliferation of EBV transformed and Burkitt lymphoma cell growth could be rapidly decreased over a short-time interval. This supports a specific, yet generally applicable therapy for C-MYC deregulated tumors in lymphomas mimicking high morbidity and mortality posttransplant lymphoproliferative disorders.

Scientific Session V: Congenital Anomalies and Neonatal Critical Care

44 THE LAPAROSCOPIC APPROACH TO THE MANAGEMENT OF CONGENITAL HYPERINSULINISM OF INFANCY (6 MINUTES)

<u>Agostino Pierro, M.D.</u>¹, Virpi Smith, Ph.D.¹, Keith Lindley, M.D.², Peter Hindmarsh, M.D.², Mehul Dattani, M.D.², Khalid Hussain, M.D.¹, ¹Institute of Child Health and Great Ormond Street Hospital for Children, London, United Kingdom, ²Great Ormond Street Hospital for Children, United Kingdom.

PURPOSE:

Congenital hyperinsulinism (CHI) is a result of either *focal* or *diffuse* pathologies within the pancreas which require different surgical and medical management. Current techniques to differentiate *focal* and *diffuse* disease are highly invasive and insensitive. During the last 18 months we used laparoscopy to perform biopsies of the pancreas and subtotal pancreatectomy. The aim of this study is to analyse the results of this minimally invasive approach.

METHODS:

The clinical course of infants with CHI who underwent pancreatic laparoscopic biopsies in a single centre was prospectively recorded. For the laparoscopic biopsy approximately 1 cm³ of the tail was excised. For the laparoscopic subtotal pancreatectomy the pancreas was resected at the right side of the superior mesenteric vessels. Results are reported as median and range.

RESULTS:

Twelve infants with CHI underwent laparoscopic biopsy of the pancreas at 16 weeks (6-104) of age with a weight of 6.0 Kg (4.5-9.5) and no focal lesions were seen. In five infants histology showed islets with normal size nuclei (suggestive of a *focal* lesion elsewhere): all were stabilised on either Octeotride and/or Diazoxide. Large nuclei suggestive of *diffuse* disease were seen in seven (atypical disease in one). Three infants underwent subtotal pancreatectomy (one laparoscopic) which confirmed the *diffuse* disease. In two no further treatment was required and one patient developed diabetes mellitus. The remaining four have mild disease and require Octeotride therapy. Enteral feeds were resumed 24 hours after the laparoscopic procedures. There were no postoperative complications.

CONCLUSIONS:

Laparoscopic pancreatic biopsy is a new, safe and sensitive method for differentiating *focal* and typical *diffuse* forms of CHI. It reduces the need for pancreatic venous sampling, intraarterial calcium stimulation test and frozen section biopsies at the time of pancreatectomy. Subtotal pancreatectomy can be safely performed laparoscopically.

45 VACUUM ASSISTED CLOSURE (V.A.C.): A NEW METHOD FOR TREATING PATIENTS WITH OMPHALOCELE (3 MINUTES) <u>Kandice E. Kilbride, M.D.</u>, Donald R. Cooney, M.D., Monford D. Custer, M.D., Texas A & M - Scott and White, Temple, TX, U.S.A.

INTRODUCTION:

Neither silo, skin flap or primary closure has been successful in treating all patients with giant omphalocele. The Vacuum Assisted Closure device (V.A.C.) allows for improved results in difficult cases.

METHODS:

The V.A.C. device (KCI, San Antonio, TX) consisted of a sponge applied directly to the bowel and liver, covered with impermeable transparent dressing, and attached to a low negative pressure system. The sponge was changed every 3-5 days under local sedation.

PATIENTS:

All three patients had giant omphaloceles. The first infant, a 34 WGA male, was initially treated with silo reduction, which disrupted after 21 days. The large mass of bowel and liver made primary closure impossible. The V.A.C. was applied for 45 days. The viscera was easily reduced, and subsequently covered with acellular dermal matrix (AlloDerm). The V.A.C. was reapplied, and the small remaining defect was skin grafted. The second baby was a 34 WGA male infant who became septic after failure of prosthetic mesh closure. The V.A.C. was applied for 22 days after removal of the mesh. The infection resolved, and the defect size was reduced, allowing for skin flap closure. Mesh infection in the last patient, a 37 WGA female child, was treated by mesh removal and application of the V.A.C. for 36 days.

RESULTS:

V.A.C. was associated with (1) rapid shrinkage and reduction of the viscera (22-45 days); (2) cleansing of the wound; (3) excellent granulation; (4) maintenance of a sterile environment; and (5) ease of use, with changes possible at the bedside.

CONCLUSIONS:

The Vacuum Assisted Closure device should be considered in difficult/complicated cases of giant omphalocele and offers a superior approach to traditional methods.



Underlining denotes the author scheduled to present at the meeting.

46 THE USE OF HUMAN ACELLULAR DERMIS IN THE OPERATIVE MANAGEMENT OF GIANT OMPHALOCELE* (3 MINUTES) Stenhanie A. Kanfer, M.D., Tamir H. Keshen, M.D., Washington, University, School of

<u>Stephanie A. Kapfer, M.D.</u>, Tamir H. Keshen, M.D., Washington University School of Medicine, St. Louis Children's Hospital, St. Louis, MO, U.S.A. * Author received a travel grant from LifeCell Corp.

PURPOSE:

The management of neonates with giant omphalocele (dia.≥7cm) presents a major challenge to pediatric surgeons. Delayed closure by SILASTIC[®] silo, polytetrafluoroethylene graft, skin flaps, or topical treatment is commonly performed. Wound infection, fascial separation, loss of abdominal domain, and other complications frequently occur, adding significant morbidity to patients with concomitant cardiac defects, pulmonary immaturity, or other congenital anomalies. Human acellular dermis (AlloDerm[®]) has been successfully used as an abdominal fascial substitute in adults. We present our experience of its application in neonates with giant omphalocele.

METHODS:

Charts of patients with giant omphalocele from January 2003 to September 2004 were reviewed and data collected regarding wound healing, rate of infection, ventilatory support, and outcome.

RESULTS:

Three neonates underwent abdominal wall closure with AlloDerm[®], covered by cadaveric skin in two and skin flaps in one (gestational ages: 38, 37, 28 weeks; birth weights: 2880g, 2640g, 1160g respectively). All had cardiac anomalies; one required cardiac surgery and one was ventilator dependent secondary to pulmonary hypoplasia. Omphalocele repair was performed on day-of-life 9, 2, and 87. Two patients were extubated within a week. No fascial dehiscence or infection was encountered. Vascular ingrowth, demonstrated by bleeding from the AlloDerm[®], was noted by day 7. Two patients died of their cardiopulmonary disease (6 months, 1 year). The third patient has exhibited normal growth and development without evidence of hernia or loss of abdominal domain.

CONCLUSIONS:

Expeditious primary closure of giant omphalocele is possible without the complications commonly seen with established treatment modalities. In our experience, AlloDerm[®] provided coverage of the abdominal viscera without compromising cardiopulmonary function, diminishing abdominal domain, or requiring multiple operations. This allowed for prompt, aggressive treatment of associated anomalies. AlloDerm[®] represents an exciting alternative in the treatment of giant omphalocele. Further study is required to determine long-term benefits.

47 PROGNOSTIC FACTORS IN SURGICAL TREATMENT OF CONGENITAL TRACHEAL STENOSIS (CTS) AND A MULTI-CENTER ANALYSIS OF THE LITERATURE (3 MINUTES) <u>Priscilla P. Chiu, M.D., Ph.D.,</u> Derek Stephens, M.Sc., Vito Forte, Peter C. W. Kim, M.D., Ph.D., The Hospital for Sick Children, Toronto, ON, Canada.

PURPOSE:

CTS is an infrequent yet life-threatening condition, often requiring urgent surgical intervention. Here, we report our recent series of CTS patients over an 18-month period and a review of the literature to determine prognostic factors relating to primary (mortality) and secondary (complications) outcomes following surgical repair of CTS.

METHODS:

Sixteen consecutive cases of CTS between 2002 and 2004 were reviewed at our institution. Multi-center published series that provide primary data on CTS patient demographics, complications and outcomes were also analyzed. Univariate, model fit and multivariate logistic regression analyses were performed using SAS[©] statistical program.

RESULTS:

Fifty-eight patients were treated by either cartilage patch tracheoplasty (n=21) or slide tracheoplasty (n=37). Patient age ranged from one day to 15 years. There were 17 deaths (overall mortality= 29%). Eight cartilage patch tracheoplasty patients died (38% mortality) compared to nine following slide tracheoplasty (24% mortality, p=0.078). Seven of 10 patients with CTS repair at or less than one month of age died (70% mortality) whereas only 10 of 48 CTS patients age greater than one month died (21% mortality) (p=0.0049). Seventeen CTS patients had co-morbid intra-cardiac anomalies. Of these, 10 died following CTS repair (58% mortality). Only seven of 41 CTS patients without intra-cardiac anomalies died and had the highest survival rate in all centers (17% mortality) (p=0.0025).

CONCLUSIONS:

To our knowledge, this is the first report analyzing prognostic factors determining the outcomes for CTS. The highest mortality was observed in CTS patients under one month of age and in patients with intra-cardiac anomalies. There was a trend toward increased mortality for cartilage patch compared to slide tracheoplasty. No differences were detected in mortality rate between individual centers but increased complications were detected between centers (p=0.04), perhaps reflecting a reporting bias in complications.

48 RISK FACTORS FOR MAJOR VENOUS THROMBOEMBOLIC EVENTS AMONG CHILDREN UNDERGOING ABDOMINAL SURGERY (3 MINUTES) <u>Randall S. Burd, M.D., Ph.D.,</u> Marissa D. Newman, B.S., Stacey B. Trooskin, MPH, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ, U.S.A.

PURPOSE:

Because deep venous thrombosis (DVT) and pulmonary embolism (PE) are rare after abdominal procedures in children, recommendations for prophylaxis have not been defined. The purpose of this study was to use a large national database to identify potential risk factors for DVT and PE and determine their relative impact on these events.

METHODS:

Records of children (<19 yrs) undergoing a major abdominal or pelvic procedure between 1995 and 2002 were obtained from the National Inpatient Sample, an administrative database containing 11 million pediatric discharge records from 36 states. Potential risk factors for a major thromboembolic event were identified using ICD-9 codes and analyzed using multivariate logistic regression.

RESULTS:

Among 192,490 children undergoing an abdominal procedure, 262 (0.14%) were identified with a DVT and 52 (0.027%) with a PE. All-cause mortality of children with a DVT was 8% and of those with a PE was 13%. Age >14 yrs was an independent risk factor for both DVT (odds ratio [OR] 1.4; 95% CI 1.1-2.0) and PE (OR 4.2; CI 2.0-8.7). The strongest predictors for DVT included a history of venous thrombosis (OR 13.9; CI 1.8-105.1), sepsis (2.7; CI 4.1-6.0), and the presence of a central venous catheter (5.4; CI 4.1-7.2), while the strongest predictors for PE included history of venous thrombosis (OR 40.4; CI 5.0-325.0), nephrotic syndrome (OR 18.0; CI 4.1-78.8) and recent stroke (OR 7.7; CI 1.8-33.4). Among children with no risk factors, a DVT was observed in 0.016% (1:6,079 patients) and a PE in 0.0061% (1:16,286 patients).

CONCLUSIONS:

In the absence of risk factors, DVT/PE prophylaxis is not needed for children undergoing abdominal surgery. Prophylaxis is most appropriately used for children with specific underlying medical conditions increasing the likelihood of venous thrombosis.

49 AORTOILLIAC RECONSTRUCTION USING BRANCHED PULMONARY ARTERY ALLOGRAFT (3 MINUTES) <u>Rebecka L. Meyers, M.D.</u>, John A. Hawkins, Larry W. Kraiss, University of Utah, Salt Lake City, UT, U.S.A.

BACKGROUND:

Aortic reconstruction in infants and small children has been reported with Dacron or PTFE prosthetic material, hypogastric artery autograft, and saphenous vein autograft. Autograft may be preferable because of growth and infection concerns with prosthetic grafts. However, the length and diameter of available arterial and venous autograft is extremely limited in babies and small children. When the entire infrarenal aorta and aortoiliac bifurcation must be replaced none of the historic options is optimal.

METHODS:

We report two cases of infrarenal aorta and aortoiliac bifurcation reconstruction using cryopreserved, decellularized branched pulmonary artery allograft. The first case is a newborn infant with a 5 cm congential abdominal aortic aneurysm with extensive intramural thrombosis of the aortic aneurysm and a concern for distal emboli. The infrarenal aorta and aortoilliac bifurcation were reconstructed with tandem aortic arch and branched pulmonary artery allografts. The second case is a four-year-old with an Organ of Zuckerkandel neuroblastoma primary tumor encasing the infrarenal aorta and bifurcation. Circumferential fibrotic contraction of the tumor following chemotherapy destroyed the aortic bifurcation necessitating resection and reconstruction with a branched pulmonary artery allograft.

RESULTS:

The postoperative course in both cases has been unremarkable. Follow-up with serial abdominal duplex ultrasound has shown no evidence of graft stenosis and/or calcification at 29 and 32 months respectively.

CONCLUSIONS:

The use of commercially available, decellularized and antigen-reduced, allograft offers a non-synthetic option for replacement of the abdominal aorta. We chose this novel approach in hopes of reducing the lifetime risk of graft infection and maintaining the potential for graft growth with the child.

50 SEVERE PULMONARY HYPOPLASIA ASSOCIATED WITH GIANT CERVICAL TERATOMAS (3 MINUTES)

<u>Kenneth W. Liechty</u>, Holly L. Hedrick, M.D., Mark P. Johnson, M.D., R. Douglas Wilson, M.D., Eduardo D. Ruchelli, M.D., Lori J. Howell, R.N., M.S., Timothy M. Crombleholme, M.D., Alan W. Flake, M.D., N. Scott Adzick, M.D., The Children's Hospital of Philadelphia, Philadelphia, PA, U.S.A.

PURPOSE:

The use of the *ex utero* intrapartum treatment or EXIT procedure in the delivery of fetuses with giant neck masses has salvaged many fetuses in which an airway would have been unattainable using standard delivery techniques. This study examines a subset of these patients who, despite an adequate airway, died as a result of an inability to oxygenate the patient.

METHODS:

We reviewed our experience with the EXIT procedure in fetal neck masses from 1996 to 2004. We have used the procedure to deliver 23 fetuses with large neck masses, either cervical teratomas or lymphangiomas.

RESULTS:

Three fetuses with giant cervical teratomas expired as a result of severe pulmonary hypoplasia and the inability to be oxygenated. On post-mortem examination these three patients had severe distortion of the airway by the mass. In these patients the carina was retracted superiorly to the level of the first or second rib by the anterior displacement of the trachea by the mass. This resulted in compression of the lungs in the apices of the chest, a vertical orientation of the mainstem bronchi, and pulmonary hypoplasia. The hypoplasia was reflected in the lung weights of 24g vs. 38g and 17g vs. 34g for age-matched normal lung.

CONCLUSIONS:

Unsuspected obstructive fetal neck masses have often proved fatal due to an inability to secure an airway at the time of delivery. Prenatal ultrasonography has been useful in the identification of fetuses at risk for perinatal airway obstruction, allowing the fetus to be salvaged using the EXIT procedure. Despite obtaining airway control, a subset of these patients will expire as the result of pulmonary hypoplasia. When counseling patients with large cervical masses it is important to discuss potential pulmonary hypoplasia in these patients.

51 RELATIVE VALUE UNITS CORRELATE WITH PEDIATRIC SURGEONS' OPERATING TIME: WHEN PERCEIVED MYTH BECOMES REALITY (3 MINUTES) <u>Danny C. Little, M.D.</u>, Shawn D. St. Peter, M.D., Casey M. Calkins, M.D., George K. Gittes, M.D., Daniel J. Ostlie, M.D., Charles L. Snyder, M.D., Children's Mercy Hospital, Kansas City, MO, U.S.A.

PURPOSE:

In 1992 Congress implanted a Medicare payment system based on relative value units (RVUs). Today, RVUs are increasingly used to determine reimbursement from Medicare, Medicaid and private third party payers. Accounting for geographic and malpractice differences, the total RVU is then multiplied by a conversion factor to set physician reimbursement. With efficiency in the operating room currently at a premium, we evaluated the hypothesis that RVUs accurately reflect the quantity of time that surgeons spend operating.

METHODS:

Over a 12-month period (1/03-12/03), 59 common, high-volume pediatric operations were identified and classified as general surgery (n=34), urology (n=13), or minimally invasive (n=10). CPT codes were reviewed and referenced to their corresponding RVU. Only operations performed as an outpatient or requiring less than one inpatient day of direct surgeon involvement were included. Through linear regression, correlation coefficients were generated comparing average operating time per procedure to RVU generated. Statistical evaluation was carried out by univariate and regression analysis.

RESULTS:

Of 59 specific types of operations, a total of 744 general surgery cases, 1,155 urologic cases, and 370 minimally invasive cases were performed. RVU efficiency was greatest in general surgery (one RVU = 5.18 operating minutes) followed by minimally invasive operations (one RVU = 6.80 minutes). Urologic operations were least efficient with each RVU generated averaging 8.59 minutes. However, regression analysis proved minimally invasive operations to correlate best with RVUs with R² = 0.8376, followed by urology at R² = 0.6753, then general surgery at R² = 0.649. There were no statistical differences between the groups.

CONCLUSIONS:

The RVU has emerged as the most dominant factor influencing reimbursement of practicing pediatric surgeons. Despite common surgeon bias, RVUs do correlate with current operating times. This data proves important as surgeons analyze cost, negotiate revenues, and strategically plan for fiscal success.

(graphic on next page)

Underlining denotes the author scheduled to present at the meeting.



52 TPN-ASSOCIATED HYPERGLYCEMIA CORRELATES WITH PROLONGED MECHANICAL VENTILATION AND HOSPITAL STAY IN SEPTIC PREMATURE INFANTS (3 MINUTES) <u>Diya I. Alaedeen, M.D.</u>, Michele C. Walsh, M.D., Walter J. Chwals, M.D., University Hospitals of Cleveland, Rainbow Babies and Children's Hospital, Cleveland, OH, U.S.A.

PURPOSE:

Excessive intravenous nutrient delivery has been associated with hyperglycemia, increased work of breathing, and cholestasis in critically ill patients. Pre-term infants may be especially vulnerable to complications due to respiratory immaturity. We hypothesized that the effects of TPN-associated hyperglycemia would adversely impact the clinical outcome in premature, septic infants in the neonatal intensive care unit (NICU) setting.

METHODS:

The charts of all ventilator-dependent premature infants weighing <1500g upon admission to the NICU between Jan. 1, and Dec. 21, 2002 with culture-proven sepsis and feeding intolerance requiring TPN were studied. Maximum serum glucose concentration while in the NICU was compared with duration of TPN therapy, mechanical ventilation, hospital length of stay, and survival, using Pearson regression analysis and Student t test.

RESULTS:

Thirty-seven patients who met the criteria were identified from a prospectively maintained database. The most common organism isolated was coagulase negative Staph (76%). The overall mortality was 16%. The average caloric intake for all infants during the first week following blood culture-proven sepsis was 83 ± 19 Kcal/Kg/day. The maximum serum glucose concentration (mg/dL) while in the NICU following positive blood cultures (sepsis) was positively correlated with the duration of TPN (r=0.45, p=0.005), length of dependence on mechanical ventilation (r=0.45, p=0.006), and hospital length of stay (r= 0.36, p= 0.03). The average maximum serum glucose level was significantly higher in the non-surviving infants (241 \pm 46 vs. 141 \pm 48, p<0.0001).

CONCLUSIONS:

TPN-associated hyperglycemia correlates with prolonged ventilator dependency and increased hospital length of stay in premature septic infants. Adequate glycemic control and avoidance of excessive nutrient delivery (> 60 Kcal/Kg/day) during periods of acute metabolic stress may improve outcome in this patient population.

53 THE EFFECTS OF INSULIN ON PROTEIN METABOLISM IN CRITICALLY ILL NEONATES (3 MINUTES)

<u>Hannah G. Piper, M.D.</u>¹, Patrick J. Javid, M.D.¹, Michael S. Agus, M.D.¹, Daniel P. Ryan, M.D.², Tom Jaksic, M.D., Ph.D.¹, ¹Children's Hospital Boston, Boston, MA, U.S.A., ²Massachussetts General Hospital, Boston, MA, U.S.A.

PURPOSE:

During pediatric critical illness a catabolic nutritional state predominates, marked by suboptimal protein accretion, growth impairment and delayed development. Nutritional support alone has been unsuccessful in quelling this metabolic illness. In non-stressed states insulin is a potent inhibitor of protein breakdown and augments protein synthesis. The effect of insulin administration on protein metabolism in neonates on extracorporeal life support (ECLS) is reported.

METHODS:

The study was approved by the Committee on Clinical Investigation. Eleven parenterally fed neonates on ECLS were enrolled in a prospective, randomized, crossover trial. Neonates received either a continuous insulin infusion using a hyperinsulinemic euglycemic clamp, or a control saline infusion for four hours on consecutive days. Rates of whole body protein breakdown and synthesis were quantified using ring-D5-phenylalanine and ring-D2-tyrosine stable isotopic infusions. Statistical analyses were performed using paired sample t-tests (significance at p<0.05).

RESULTS:

Serum insulin levels were increased 20-fold during insulin infusion compared to saline infusion (451 \pm 39 µU/mL vs. 23 \pm 7 µU/mL, p<0.0001) with no significant difference in plasma glucose levels. Protein breakdown was significantly decreased during insulin infusion compared to saline control (6.77 \pm 0.99 g/kg/day vs. 7.91 \pm 1.90g/kg/day p<0.05). Protein synthesis, however, was also decreased during insulin infusion compared to saline control (8.41 \pm 1.05 g/kg/day vs. 9.46 \pm 2.11g/kg/day p<0.05). The overall protein balance was 1.63 \pm 0.89 g/kg/day during insulin infusion vs. 1.54 \pm 0.81 g/kg/day during the saline control period (p=0.14).

CONCLUSIONS:

In critically ill neonates on ECLS insulin infusion significantly reduced whole body protein breakdown. However, this was accompanied by a concomitant decrease in protein synthesis. Mechanistically, the latter finding may be due to a reduction in amino acid availability engendered by decreased protein breakdown. Overall, insulin administration may have only marginally improved protein balance and this finding did not attain statistical significance.

2005 Exhibitors

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 American Pediatric Surgical Nurses Association
 Table Number: 18

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APSNA membership spans the spectrum of the care of children requiring surgical care from trauma to burns to injury prevention; from inpatient to ambulatory surgery; inpatient and outpatient care; neonatal through adolescent; NICU and PICU; the inpatient units; PACU; registered nurses and nurses in advanced practice. We are as diverse as the children we serve.

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Elsevier publishes medical books, journals and multimedia.

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Table Number: 17

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Intuitive Surgical is the leading manufacturer of surgical robotics used in minimally invasive surgical procedures.

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Table Number: 15

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Table Number: 14

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Lippincott, Williams & Wilkins has some of the latest publications in surgery. Also displaying McGraw-Hill and Springer Books.

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Table Number: 2

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Table Number: 11

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Table Number: 3

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Table Number: 12

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