



Center For Advanced Fetal Care Newsletter

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INSIDE THIS ISSUE

Oculus...	1
NIPT for DMD	1
Femoral Angle	1
Highlights AIUM	2
Highlights Bangkok	2
CFAFC Recommends	3
Abstract Submission FMF	3
Upcoming ISUOG Congress	3
Latest on ZIKAV	3
Pocket Brain	3
CFAFC News	3
Hot-off-the-Press	3
Featured Case	4
Featured Quote	4
Upcoming Courses	4

Oculus...

...Into obscurity. Seeking lucidity. Aspiring for continuity... We never know when our lives shall be **interrupted** leaving behind much that is **unfinished**. We are under the constant pressure of time in a perpetual quest for answers, for that which is in **nature** around us and far beyond, inspired by **art** and **rooted** in science. We have made **strong strides** in medicine yet are now under the direct threat of being **out-smarted** by our own inventions. We thus dedicate this issue to "oculus", the **window** to the sky, the boundless **virtual eye**. We open an "oculus" into the latest advances in fetal medicine from the NIPT of Duchenne muscular dystrophy, to the utility of the femoral angle in the prenatal diagnosis of achondroplasia. We bring you highlights from the Annual Convention of the AIUM and the 3rd Bangkok International Fetal Echocardiography Symposium which brought together global minds for the exchange of knowledge. We present to you ACOG's latest Practice Bulletins on prenatal diagnostic testing for genetic disorders and screening for aneuploidy. We introduce to you "Brain Pocket", the latest interactive tool to help in the comprehension of the perplexing developing brain. We sincerely hope that this issue illuminates our oculi into a most exciting promising tomorrow in which **gravitational waves** long believed-in are **finally heard**, where Alpha Centauri is a mere **starshot** away, where we can ultimately diagnose congenital malformations with certainty and where we can impact neonatal outcome positively...



Anselm Kiefer, Paris, RS Abu-Rustum



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Prenatal NIPT for DMD/BMD by Parks et al

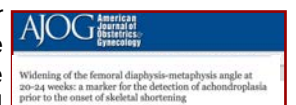
With the advances of NIPT, it is now possible to detect single gene disorders (SGD) such as B-thalassemia, congenital adrenal hyperplasia and Duchene as well as Becker muscular dystrophies (DMD/BMD) using massively parallel sequencing (MPS). However, that involves high cost. As such, in their recent work in **Prenatal Diagnosis**, Parks et al describe a novel affordable technique based on Lo et al's relative haplotype dosage (RHDO) analysis. In their study, the authors recruited a total of 7 healthy donor pregnancies and 2 pregnant DMD carriers all with male fetuses. NIPT was carried out using RHDO analysis for X-linked disorders utilizing genomic DNA extracted from CVS samples from the 2 groups in order to identify the reference haplotype. The test had an overall sensitivity of 98.7%, and when the fetal fraction exceeded 4%, the test was able to achieve a sensitivity of 100%. It was also possible to detect a recombination event in one of the DMD patients. As such, the authors conclude that in their initial validation studies, their affordable new test has proven accurate and reliable and may potentially be incorporated into clinical practice on condition that a DNA sample from the proband is available.



Non-invasive prenatal diagnosis of Duchenne and Becker muscular dystrophies by relative haplotype dosage

Femoral Angle in Achondroplasia by Khalil et al

Achondroplasia remains a challenging prenatal diagnosis particularly prior to 25 weeks of gestation. In a study by Khalil et al recently published in the **American Journal of Obstetrics and Gynecology**, the authors describe the role of the femoral diaphyseal-metaphyseal angle (DMA) in the prenatal diagnosis of achondroplasia at 20-23 weeks. The case-control study included 164 normal fetuses and 4 with achondroplasia. The DMA was prospectively measured on the normal fetuses between 20-23 weeks while ensuring an insonation angle of less than 45°. For the affected fetuses, the DMA was measured retrospectively using stored images of the femoral length measurements. There was a statistically wider DMA in fetuses with achondroplasia in comparison to controls with a P < 0.001. A wide femoral angle of ≥ 120 degrees was found in all 4 fetuses with achondroplasia. The authors conclude that though larger prospective studies are needed, a wide femoral angle may potentially be used as a second trimester screening marker for achondroplasia.



Widening of the femoral diaphysis-metaphysis angle at 20-24 weeks: a marker for the detection of achondroplasia prior to the onset of skeletal shortening

Highlights from the American Institute of Ultrasound In Medicine's Annual Convention Held 17-21 March 2016 in New York City

An outstanding **AUIM Annual Convention** took place in NYC March 17-21, 2016 where probe-handlers from various disciplines gathered for 5 amazing days in vibrant NYC. The organizing committee had put together a wonderful program commencing with a day of pre-congress courses and 4 days of over 120 sessions covering every imaginable aspect of ultrasound.

This year witnessed the first "SonoSlam", a competition put forth for medical students, and it received raving reviews. SonoSlam was held on the day of the pre-congresses and 16 teams from various medical school across the country competed for the "Peter Arger Cup". The AIUM encourages all medical schools supporting ultrasound in medical education to start planning for next year's competition, which promises to be even bigger! The pre-congress courses were varied and comprehensive, particularly "Fetal Imaging in Early Gestation: A Comprehensive Review". This course was directed by Profs. Abuhamad and Wilkins and had an outstanding group of speakers who covered image optimization, pregnancy dating and viability, pregnancy of unknown location, fetal anatomy including the fetal heart and neurosonogram among many others. The plenary session was unforgettable with Prof. Timmerman, delivering the William J. Fry Memorial Lecture "Tips & Tricks of Successful Ultrasound Studies" and Prof. Abuhamad delivering an inspiring plenary talk "Global Maternal health: Ultrasound and Access to Care". The remainder of the convention encompassed basic as well as advanced sessions and abstract presentations on the latest research in medical education, obstetrics, fetal echocardiography, gynecology among many others. The hands-on sessions were well received and a highlight for many attendees.

Lebanon was well represented with 6 abstracts which were the result of wonderful collaboration between S & R Abu-Rustum, L Daou, N Helou, G Mahmoud, J Ward and F Ziade.

For more details on and reviews of the 2016 convention, visit "**The Scan**". Plans are currently underway for the next AIUM Convention to be held in Orlando March 25-29, 2017. For further information, stay tuned to the **AUIM Website** for abstract submission and registration.



AIUM 2016



Prof. Mastrobattista

Highlights from the 3rd Bangkok International Fetal Echocardiography Symposium Held 18-20 January 2016 in Bangkok, Thailand. By Mark Sklansky, MD

The 3rd Bangkok International Fetal Echocardiography Symposium, held in the majestic Dusit Thank Bangkok Hotel in the heart of Bangkok (January 18-20, 2016), brought together well over a hundred subspecialists from around the world for three days of state-of-the-art presentations and discussions, live hands-on scanning, and mingling/networking with colleagues, new and old. The symposium provided a clinically oriented series of presentations and lively discussions of topics related to fetal cardiac imaging, diagnostics and management. This third year of the symposium attracted pediatric cardiologists, obstetricians, maternal-fetal medicine and other affiliated subspecialists from throughout Southeast Asia and beyond, including over 35 attendees from Malaysia, Indonesia, the Philippines, India, the Maldives, Vietnam, Cambodia, Nepal, Hong Kong, Myanmar, Japan, Taiwan, the U.K. and the United States, as well as from throughout Thailand.

The first of the symposium's three days began with a series of talks on the current approach to fetal cardiac screening, including an update on guidelines and approach to the segmental diagnosis of congenital heart disease. An expert panel then discussed various approaches to prenatal screening around the world. A series of talks on abnormalities of the outflow tracts and of pulmonary venous return was presented after lunch, followed by live-scanning by Dr. Sharland and a hands-on scanning session for attendees. Day two began with presentations on critical forms of congenital heart disease (hypoplastic left/right heart syndromes), as well as heterotaxy and common abnormalities of the foramen ovale, ductus arteriosus and ductus venosus. Afternoon talks focused on perinatal interventions and counseling, followed by a live-scanning by Dr. Sklansky and additional hands-on scanning by registrants. The third and final day included presentations on fetal arrhythmias and cardiac function, followed by panel discussions on how to set up a fetal heart program and how to minimize medical-legal problems. The symposium ended with an overview on pitfalls and pearls of fetal cardiac imaging by Dr. Sklansky.

Given the glowing reviews from this third international fetal symposium, plans are already underway for next year's exciting and innovative symposia, currently planned for the week of January 9-13, 2017, with the first two days dedicated to fetal cardiology, the third day addressing the fetal-adult continuum of CHD, and the last two days dedicated to adults with congenital heart disease. For more details, please contact Dr. Limsuwan (alimsuwan@yahoo.com) or visit the symposium's **website**.

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Drs. Sklansky, Sharland, Hseih & Yasukochi



Live Scan with Drs. Yasukochi & Promsonthi

CFAFC Recommends: ACOG's Latest Technical Bulletins

ACOG in collaboration with the **Society of Maternal Fetal Medicine** has recently released 2 revised Practice Bulletins: "Prenatal Diagnostic Testing for Genetic Disorders" and "Screening for Fetal Aneuploidy". The practice bulletins were just published in the May issue of **Obstetrics and Gynecology**.

"**Prenatal Diagnostic Testing for Genetic Disorders**" reviews the current status of prenatal genetic testing in addition to covering the evidence in support of its use. It addresses invasive as well as non-invasive procedure, preimplantation genetic diagnosis and various concerns as to whom to offer testing to, when to perform the testing and which tests to choose. In addition, it covers such challenging topics as how to discuss variants of unknown significance with the patients, what testing to offer in the case of multiple gestations and it explains which test may uncover underlying mosaicism. It offers new insight on the role of microarrays in the context of sonographic findings and in the case of in utero fetal demise. The bulletin includes a comprehensive table detailing the various testing modalities and concludes with a series of recommendations.

"**Screening for Fetal Aneuploidy**" provides a comprehensive overview of all screening modalities for aneuploidy addressing their benefits, sensitivities and limitations. It introduces the "penta screen" which includes hyperglycosylated HCG in addition to the constituents of the quad screen. This bulletin has a summary table detailing all screening modalities for aneuploidy as to gestational age for performing the tests, sensitivities, false positive rates, advantages and disadvantages. It also provides a summary table of management guidelines based on the presence of soft markers on sonographic evaluation.

CFAFC highly recommends these up-to-date comprehensive Practice Bulletins for all clinicians involved in patient counseling.



THIS AND THAT

FMF Abstract Submission



Abstract submission is now open for the **FMF's 15th World Congress** to be held in Palma de Mallorca, Spain June 26 - 30, 2016. As usual, this congress promises to bring together world leaders for an intense 5 days (sunrise to sunset) filled with presentations and discussions pertaining to the latest advances in the field. The level of interaction is unparalleled in an amazing atmosphere of comradery. For details, visit the **FMF Website**.

ISUOG World Congress



ISUOG continues its 25th anniversary celebrations with its upcoming **World Congress** to be held in Rome September 25-28, 2016. This year, a record number of abstracts, 1200 in total, has been submitted promising a rich congress with the latest cutting-edge research. In addition, there will be various workshops and plenaries given by luminaries in the field, and the chance to spend time in majestic Rome. Details at the **ISUOG Website**.

ZIKAV in the News



As the evidence continues to accumulate in support of the "Zika Virus Syndrome" numerous global organizations and societies have put forth guidelines and recommendations covering background information, modes of viral transmission to the mother and subsequently the fetus, diagnostic modalities, sonographic findings and management. For some of the latest recommendations, check out the most recent guidelines from **WHO, CDC, ISUOG, ACOG** and **SMFM**.

Pocket Brain



An ingenious new tool has been created by Profs. Tutschek and Pilu, world class educators and experts on fetal neurosonography. "**Pocket Brain**" was just reviewed in **UOG** and may be accessed with the password "vr". It puts the normal and abnormal fetal brain at ones' fingertips providing detailed beautifully labelled images that can be scrolled through and carried on smart phones. Dr. Tutschek welcomes feedback at tutschek@me.com.

CFAFC News



It has been a most memorable spring for **CFAFC's** Reem S. Abu-Rustum. She received the "**Shield of Honor**" of **Lebanese Order of Physicians**. She was elected Secretary of the **AIUM Obstetrical Ultrasound Community**. She served as a member of the **WHO Interim Guidance** development group on pregnancy in the context of Zika virus disease, and served as co-editor of **ISPD's Prenatal Perspectives**. She was an invited speaker at the **AIUM Annual Convention** in NY by the Fetal Echocardiography Community. She is ever so grateful for all these opportunities...

Hot-Off-The-Press



ISUOG's Practice Guideline addressing the role of ultrasound in the management of twin gestation has been published in the February issue of **Ultrasound in Obstetrics & Gynecology**.

As is customary for ISUOG, a comprehensive guideline has been put together by leading experts in the field covering every imaginable aspect in twins: dating, determining chorionicity, labeling of twins, prenatal screening with respect to the detection of aneuploidy and structural abnormalities, diagnosis and management of discordance, selective reduction, screening for preterm birth, screening and management of growth restriction, management in case of an in utero demise and management of the various complications of monochorionicity.



Dichorionic Diamniotic



Conjoined

Key points to keep in mind:

- 1- It is ideal to date twins when the CRL is between 45 - 84 mm using the larger of the two CRL's.
- 2- Determine chorionicity prior to 13w6d using the lambda and T-signs. In addition, amnionicity should also be determined.
- 3- Label twins using a consistent strategy and document properly.
- 4- For uncomplicated dichorionic twins, perform a first and second trimester scans then assess every 4 weeks.
- 5- For uncomplicated monochorionic twins, perform a first trimester scan then assess every 2 weeks starting at 16 weeks onwards.
- 6- First trimester combined testing may be used keeping in mind that NIPT has a lower sensitivity in twins.
- 7- Be mindful of $\geq 10\%$ discordance in CRL or $\geq 20\%$ discordance in NT.
- 8- Cervical length screening for preterm birth may be utilized using a cut-off of 25 mm.
- 9- Use fetal head, abdomen and femur measurements to determine fetal weight. A discordance of $\geq 25\%$ warrants referral to a tertiary care center.
- 10- Selective growth restriction is when one fetus is ≤ 10 th centile and the discordance is $\geq 25\%$.

For the in depth review, the guideline is available at **ISUOG** as open access.



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CF AFC expresses its sincerest appreciation to Drs. Rayan Bou Said, Jihad Feghali, Nabil Helou, Mark Sklansky and Boris Tutschek for their contributions to this issue.

"It is the great minds who bypass normalcy and dare to do the unthinkable."

Maria Kuran

All colored text contains embedded **'clickable'** links. For any interesting case reports, comments, suggestions or announcements, please send an e-mail to rar@cfafc.org.

Extralobar Sequestration at 22W0D. Case by Drs. R. Bou Said, J. Feghali and N. Helou.

We present the case of a 24 years old female , G1 P0, who presented at 22w0d weeks for a second opinion due to a pulmonary mass noted during second trimester sonographic evaluation. She had a non-contributory past medical/surgical history and an uncomplicated prenatal course thus far.

Upon examination, there was a triangular hyperechoic lesion in the left lower pulmonary lobe (Figure 1). It had no mass effect on the surrounding lung parenchyma, diaphragm or heart. It had a central hypoechoic structure (Figure 1, *). Color Doppler assessment demonstrated direct arterial supply from the abdominal aorta with venous drainage into the inferior vena cava (Figure 2). The diagnosis of extralobar bronchopulmonary sequestration was made. The central hypoechoic structure was found to be the vascular pedicle.

Bronchopulmonary sequestration (BPS) is a very rare entity with an estimated incidence of less than 0.1 % (0.15 to 6.4% of all congenital pulmonary malformations). In the majority of cases, BPS regresses during the course of pregnancy, but occasionally, it may lead to hydrops fetalis as a result of vascular compression.

BPS consists of nonfunctional pulmonary tissue which is usually cystic and mass-like. The abnormal parenchyma receives abnormal blood supply, usually from the aorta, and has no communication with the tracheobronchial tree. Both forms of BPS, intralobar and extralobar, occur most commonly in the posterior basal segment of a lower lobe, usually the left lobe. Intralobar sequestration is contiguous with normal lung parenchyma and has no separate pleural investment unlike extralobar sequestration, which is separated from normal parenchyma by a pleural surface and sometimes the diaphragm. Other differences between intralobar and extralobar BPS are summarized in the table below.

	Intralobar	Extralobar
Arterial Supply	Aorta	Aorta
Venous Drainage	Pulmonary	Systemic (IVC, azygos or portal)
Associated Anomalies	Rare	Frequent (paralysis/ eventration of ipsilateral diaphragm, diaphragmatic hernia)
Pleural Investment	Contiguous with normal lung	Separate
Gender Distribution	Equal	Male predominance
Relative Frequency	75-90%	10-25%

As our case demonstrates, BPS is usually an incidental second trimester finding of a well-delineated homogeneous echogenic pulmonary mass. The mass may be small or it may occupy the entire hemithorax, frequently resulting in a mediastinal shift. The key to its diagnosis is demonstrating an abnormal arterial supply to the mass from the aorta, utilizing color flow Doppler, as was evident in our case. If a feeding vessel cannot be visualized, the extralobar sequestration may appear identical to an echodense microcystic congenital pulmonary airway malformation (CPAM). In such a case, MRI may help ascertain the diagnosis.



Figure 1



Figure 2

Upcoming Congresses

COURSE TITLE	DATES	LOCATION	WEBSITE ADDRESS
European Human Genetics Conference	May 21 - 25, 2016	Glasgow, UK	www.eshg.org/home2016.0.html
32nd Fetus as a Patient	May 27 - 29, 2016	Tirana, Albania	www.fetus2016.eu/pdf/scientific-program-total.pdf
ISUOG's Ultrasound in the Diagnosis and Management of Endometriosis (Live Stream)	Jun 3 - 4, 2016	London, UK	www.isuog.org/Events/ISUOG+Organised+courses/2016_June_Endometriosis.htm
RCOG World Congress	Jun 20 - 22, 2016	Birmingham, UK	www.rcog.org.uk/en/departmental-catalog/Departments/other-events/rcog-world-congress-2016/
15th World Congress of the Fetal Medicine Foundation	Jun 26 - 30, 2016	Palma De Mallorca, Spain	www.fetalmedicine.org/fmf-world-congress
20th International Conference on Prenatal Diagnosis & Therapy	Jul 10 - 13, 2016	Berlin, Germany	http://2016.ispdhome.org/
26th Annual Congress of ISUOG	Sep 24 - 28, 2016	Rome, Italy	www.isuog.org/WorldCongress/2016/
6th Annual Fetal Echo Symposium at UCLA	Oct 15, 2016	Los Angeles, CA	www.cme.ucla.edu/courses/event-description?registration_id=124261
7th Annual Fetal Echocardiography Normal and Abnormal Hearts	Nov 3 - 5, 2016	Las Vegas, NV	www.edusymp.com/product/details/890
Advanced First Trimester Ultrasound	Nov 25 - 26, 2016	Cracow, Poland	www.ultrasoundcracow.com/dates-agendas/