Center For Advanced Fetal Care Newsletter

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INSIDE THIS ISSUE

A Kaleidoscopic Look Into The Future...

Looking Through The Kaleidoscope

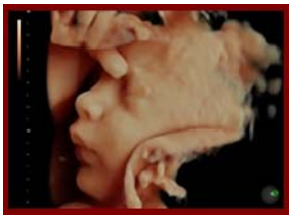


Image Courtesy of Bernard Benoit, MD

"Stunned and in awe" is how one would describe the general atmosphere in the grand hall at the most recent 21st Annual Congress of ISUOG in Los Angeles as Dr. Bernard Benoit worked his magical kaleidoscope and took us on a unbelievable journey into the future of 3D/4D ultrasound and unveiled "HDLive" to the world. Never has the impact of the "power of vision" been as palpable as it was when one got to experience the looks on the faces of the world's experts as they feasted their eyes on the masterpieces of Benoit...The babies were vibrant, their breaths could almost be felt, to the point where, according to Benoit, the mothers felt scared as their in-utero babies were just "too real". And this is where we are going, where the future is taking us, further into the realm of what was previously intangible, enabling us to discover more and more, and at much earlier gestations, with unfathomable clarity, and with more and more certainty...With this issue, we hope to give you a sneak peak through the kaleidoscope, into the future of our specialty. We bring you the latest breakthrough research on fetal aneuploidy detection from maternal plasma DNA that shall revolutionize prenatal diagnosis as we have come to know it, in addition to select abstracts from the "Pregnancy Meeting" of the SMFM. We present to you the future of volume sonography with its rising role, way beyond the pretty face, as exemplified by the work of the visionary group from EVMS, inspired by Abuhamad's Z-Technique, promising to change the global approach to the work-up of suspected mullerian abnormalities. We present to you research from Lebanon, in addition to our usual quarterly features. We hope that with this kaleidoscopic glimpse into the future, the magical spell shall be cast, further propelling us in our quest for unraveling the mysteries of the unknown...

Genome Wide Fetal Aneuploidy Detection From Maternal Plasma DNA

One of the highlights of the "Pregnancy Meeting" was the futuristic prospective, blinded multicenter trial by Bianchi et al on the diagnostic accuracy of genome wide fetal aneuploidy detection by sequencing of maternal plasma DNA. Massively parallel sequencing (MPS) of maternal plasma DNA was carried out on blood samples collected from 2882 women, with both normal and abnormal karyotypes (ratio 4:1), undergoing prenatal diagnostic procedures. All samples underwent evaluation for each of chromosomes 21, 18, 13, male, female and monosomy X. The results were compared to the fetal karyotype. From 532 samples with an abnormal karyotype, MPS was able to detect 89/89 trisomy 21, 35/36 trisomy 18, 11/14 trisomy 13, 232/233 females, 184/184 males and 15/16 monosomy X with no false positives in the normals. Furthermore, MPS was able to detect all cases of mosaicism, translocation trisomy, autosomal trisomy and other sex chromosome aneuploidies. The authors conclude that MPS provides superior sensitivity and specificity to serum analytes and ultrasound in the diagnosis of trisomy 21 and 18, and is capable of detecting trisomy 13 and monosomy X. This will ultimately revolutionize the future of prenatal diagnosis and further minimize the need for invasive testing.

Elastography Of The Cervix In Pedicting Successful Induction

Elastography is a promising novel sonographic technique that measures tissue deformity in response to pressure application. Utilizing special sonographic software, the rate of deformity to the pressure applied through the transducer may then be displayed as a color map to differentiate tissue consistency: soft tissue tends to deform more (maps as red) than hard tissue (maps as purple). Two recent studies have evaluated the role of elastography of the cervix. The first study by Swiatkowska-Freund and Preis found it a useful method in evaluating cervical ripeness and predicting a successful induction (http://onlinelibrary.wiley.com/doi/10.1002/uog.9021/pdf). However, a more recent study by Molina et al (http://onlinelibrary.wiley.com/doi/10.1002/uog.11067/pdf) suggests that it may be variations in operator-induced pressure and not the tissue characteristics that may be giving us the varied color map. Both conclude that the technique is of utility, however, it may still be too premature to base clinical decisions on the results and more time and experience with the technique is needed.

Select Abstracts from the Society of Maternal Fetal Medicine's Annual Meeting in Dallas, February 6-11, 2012

A landmark annual "Pregnancy Meeting" of the SMFM was held in Dallas with over 800 abstracts presented. A most enlightening pre-congress course program highlighted the critical areas in the specialty: maternal critical care, fetal echocardiography, genetics in clinical practice, infectious disease update to name a few...We hereby provide a brief overview of select abstracts and oral communications presented. Complete abstracts can be found in the American Journal of Obstetrics and Gynecology (The Grey Journal) January 2012, Volume 206, Issue 1, Supplement. In addition, all abstracts are available on the newly released AJOG iPad app (currently for free during the trial period and highly recommended by CFAFC).

A Multicenter Prospective Masked Comparison Of Chromosomal Microarray With Standard Karyotyping For Routine And High Risk Prenatal Diagnosis. Roland Wapner.

The aim of this study was to evaluate the role of chromosomal microarray (CMA) as an independent method for prenatal cytogenetic diagnosis. 31 centers sent amniotic and chorionic villi samples, from 4401 patients, to a central karyotyping lab. 46% were advanced maternal age (AMA), 18% with abnormal 1st or 2nd trimester screening, 26% with an abnormal ultrasound and 9% for other indications. All samples were divided into two: karyotype was performed on one portion and the second was sent to one of 4 independent labs for CMA. For the CMA, there were 84 regions of known associated disease (43 centromeric and 41 telomeric regions). Karyotype and MCA results were reported to an independent center. Any microdeletions or duplications that were identified exclusively by MCA were labeled as "of known clinical significance" or "benign" in accordance with predefined listings. All other copy number variants (CNV) were labeled as "of uncertain clinical significance". In 98.7% of samples, CMA was successful. Most notably was that in 5.8% of cases with a normal karyotype but with an abnormal ultrasound, and in 1.7% with AMA or positive screening, CMA identified a microdeletion or duplication, of potential or known clinical significance, stressing the invaluable role of CMA.

Prenatal Treatment Prevents Learning Deficit In Down Syndrome Model. Kari Horowitz et al.

This was a study to evaluate if prenatal treatment with neuroprotective peptides (NAP + SAL) may prevent learning deficits in Down Syndrome mice (Ts65Dn mice). The mice were randomly assigned to either receive prenatal peptides or placebo. Subsequently, the offspring were assessed postntally in their ability to find the platform in a watermaze and how much time they required to accomplish that. The peptide-treated mice had statistically significant learning abilities in comparison to those that received placebo and the peptide-treated mice were similar to normal controls. This study, as the authors concluded, holds great promise that there is a possibility of halting the sequelae of Down's Syndrome and that there is a promising role for prenatal intervention.

Does Fetal MRI Impact Clinical Decision Making Of Ultrasound-Diagnosed Fetal Lesions? A Center's 10 Year Experience. Jeanine Carbone et al.

This was a retrospective study on 328 patients, with a sonographically diagnosed anomaly, in an attempt to determine whether fetal MRI provided any additional information to prenatal ultrasound and whether that had any impact on clinical management. The primary indication for fetal MRI was a suspected CNS abnormality (in 53%). Fetal MRI confirmed the sonographic diagnosis in 33.2%, it added additional information in 32.3%, it changed the sonographic diagnosis in 22.6% and changed the diagnosis to normal in 11.9%. Overall, MRI changed the clinical management in 61.9% leading the authors to conclude that fetal MRI has a complementary role to fetal ultrasound and its greatest impact is in prenatal counseling.

Patterns Of Compromised Fetal Brain Growth In Congenital Heart Disease. Turan et al.

Children with congenital heart disease (CHD) are at risk for neurodevelopmental delay due to compromised prenatal head growth that leads to small brain volumes. The authors sought to characterize the relationship between the type of CHD and its associated cardiovascular dynamics, and fetal brain growth. They evaluated 89 chromosomally normal fetuses with CHD and 1535 normal controls. All had head circumference, brain volume, fetal cephalization index, growth potential and middle cerebral artery pulsatility index (MCA PI) measured. There were 7 with transposition of the great arteries (TGA), 55 with hypoplastic left heart and critical aortic stenosis with retrograde flow at the aortic isthmus, 14 with pulmonary stenosis, Tetralogy of Fallot and tricuspid atresia, and 13 with left ventricular outflow obstruction with net antegrade isthmic flow. The left sided lesions and TGA were associated with significantly smaller head size but not all could be explained by middle cerebral artery sparing. The authors conclude that prenatal evaluation of central hemodynamics may become critical in cases of CHD for predicting neurodevelopmental risk in order to direct prenatal interventions.

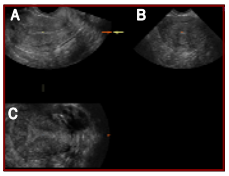
Quantification Of Ultrasound Umbilical Vein Changes In Fetal Diaphragmatic Hernia. Douglas Richards and David Kays.

The prognosis of fetuses with congenital diaphragmatic hernias (CDH) is dependent, in a large part, on whether or not there is liver herniation into the chest. A subjective sonographic maker to assess for liver herniation is umbilical vein deviation. As such, the authors quantify the degree of umbilical vein deviation in cases of CDH and determine its accuracy in predicting liver prolapse. This was a retrospective study over a 15 year period in which the authors first determined the normal ratio for the distance from the lateral edge of the mid-hepatic portion of the umbilical vein to the left inner rib margin versus the right (UVR). A UVR < 0.4 was shown by ROC analysis to be the best predictor for liver prolapse, with a sensitivity of 0.89 and a false positive rate of 0.14. The authors conclude that in routine screening ultrasound, this deviation may be a useful indicator for CDH.

A Targeted Approach For The Prenatal Detection Of Common Aneuploidies And 15 Microdeletion Syndromes. Lisa G. Shaffer et al.

This was a prospective evaluation employing a novel assay, utilizing Luminex xMAP system and BACs-on-Beads technology, that enables the evaluation of 5 common aneuploidies and 15 microdeletions. There were 80 clinical samples, both amniotic fluid and chorionic villi, that were all tested for karyotype as well. The assay required a mean of 1.85 days and detected 2 cases of trisomy 18, 3 cases of trisomy 21, 1 case of deletion 1p36 and 1 case of 5p15 deletion. The assay missed a 69,XXX. Another case, contaminated by maternal cells, was 45X by karyotype. Overall, the assay detected 2.5% of microdeletions that would have been missed by karyotyping. The authors conclude that in low risk-pregnancies, this assay is a viable alternative to FISH aneuploidy screening and microarray testing.

CFAFC's Technical Recommendation: The Z Technique, A 3D Gyn Technique & Its Role In Detecting Uterine Abnormalities



Back in 2006, Abuhamad et al described the Z technique, a novel sonographic technique that utilizes 3D volume datasets of the uterus, manipulates them in a standardized manner, in order to generate the mid-coronal view of the uterus (www.jultrasoundmed.org/content/25/5/607.full.pdf+html?sid=dfcfcbc3-5862-428a-9e31-8f48f8c36e8). The Z technique utilizes 4 steps in which a 3D volume of the uterus, acquired in a sagittal plane, is displayed in the 3 orthogonal planes. First, the reference/rotational dot is placed in the mid level of the endometrium in reference plane A. Second, rotation is carried out along the Z–axis in reference plane A to align the long axis of the endometrial stripe horizontally. Third, the reference/rotational dot is placed in the mid level of the endometrium in reference plane B. Fourth, rotation is carried out along the Z–axis in reference plane B to align the long axis of the endometrial stripe horizontally. Upon the completion of these 4 steps, the mid-coronal view of the uterus is automatically generated in reference plane C. And now, 5 years later, the visionary team at Eastern Virginia Medical School, headed by S. Bocca, carry out a brilliant study, supported in part by the AIUM's Endowment for Education and Research, in which they evaluate the cost, accuracy and benefits of 3D sonography in comparison to hysterosalpingography (HSG) in the workup of 101 women with uterine abnormalities (www.jultrasoundmed.org/content/31/1/81.full.pdf+html). This is of utmost importance in the workup of patients with recurrent pregnancy loss, as well as infertility, and directly impacts clinical and surgical management. The team utilized the Z technique to generate the mid-coronal view of the uterus in 101 cases suspected of a uterine abnormality. All patients underwent HSG, and surgical findings were used as the standard for definitive diagnosis. This approach provided similar or better accuracy when compared to standard HSG with lower cost and morbidity. This is a message to all of us utilizing 3D sonography: incorporating the simple Z technique to our daily practice would translate into a high sensitivity in diagnosing mullerian abnormalities, a tremendous cut in cost, better patient management and less patient morbidity.

THIS AND THAT

AIUM Annual Convention

The annual convention of the AIUM will be held March 29 to April 1, 2012 in Phoenix, Arizona. An exciting program is in the works with record numbers of submitted abstracts. In addition several in-depth pre-congress sessions are planned. For more details and to register, please visit www.aium.org/cme/events/ann2012/ann2012.aspx.

Abstract Submission ISUOG

The 22nd World Congress of the International Society of Ultrasound in Obstetrics and Gynecology will be held in Copenhagen September 9-12, 2012. A most varied program has been planned with live scan demonstrations, "meet the expert" sessions, "state of the art" lectures in addition to the newly introduced sessions for "trainees". Abstract submission is now open, and more information is available at www.isuog.org.

Abstract Submission FMF

The 11th World Congress of the Fetal Medicine Foundation is to be held on the Island of Kos, Greece June 24-28. As usual, attendees should be ready for a most intense congress. Again this year it will be held in combination with the Eurofetus meeting, as well as sessions by the Serono Symposia International Foundation. Abstract submission, registration and hotel information are available at www.fetalmedicine.com/courses-congress/conferences/.

Recommended Apps

With the ever rising number of available medical apps, it becomes quite a challenge to sort through and select the most useful apps. As such, a new app, DG App, brings you up-to-date on the newly released medical apps and lists "featured", "latest", "popular" and "rising" medical apps. CFAFC also recommends "PrenatalDates" and "Gestational Age Calculator", two apps to replace the traditional pregnancy wheel available at your fingertips in any patient encounter, that enable you to calculate due date, current gestational age in addition to determining the calendar date for each patient's iatrogenic period and various sonorgraphic and biochemical modalities. But by far, the ultimate app is the newly released "Green Journal": it is clean, crisp, seamless in navigation and puts the wealth of the Green Journal on your iPad to carry with you everywhere. In addition, the "Grey Journal" has also released an App that currently gives free access to the entire program and abstracts of the SMFM's "Pregnancy Meeting". Those apps are available at the App Store and during the trial period, the journals are available free of charge.

Reasearch From Lebanon: The Lebanese Experience With The Prenatal Diagnosis And Outcome Of Single Umbilical Artery.

By A. Kesrouani MD & S. Richa MD. Hotel Dieu de France, Beirut-Lebanon.

This abstract was presented at 9th Congress of the European Society of Gynecology in Copenhagen in 2011 (ESG/SEG 2011).

Objective: Single umbilical artery (SUA) is a rather common finding in obstetrical ultrasound that has various implications for other underlying pathology. The aim of this study was to evaluate the characteristics and outcome of fetuses with a single umbilical artery (SUA) in an unselected Lebanese population.

Methods: This was a retrospective study carried out between 2000 and 2010. All fetuses that were sonographically diagnosed to have a SUA were reviewed. Gestational age at diagnosis, side of the absent umbilical artery, antenatal investigation, pregnancy course and neonatal outcome were assessed.

Results: There were 16 cases of SUA in a population of 1260 (1.26%). The left side was absent in 9 cases (56%). Twelve cases were diagnosed at 12-13 weeks, 3 cases at 17 weeks, and one case at 32 weeks. In 2/16 with a SUA, there were other sonographic abnormalities. One case was in a dichorionic diamniotic gestation. In the other case, there was a history of a prior baby with SUA, uretral anomaly, and C21 hydroxylase deficiency. Amniocentesis was performed in 8 cases for various reasons. Most were for parental anxiety. Other indications were for an abnormal triple test and for the presence of a choroid plexus cyst. Only one case was terminated for multiple malformations, however, there was a favorable outcome in the remaining 15 cases. IUGR was diagnosed in 5 cases, and the mean gestational age at delivery was 36 weeks.

Conclusion: SUA is a common occurrence. Though it may be associated with IUGR and other pathology, the majority of isolated cases in our population have a favorable outcome. This information should be made available to the families in order to decrease undue parental anxiety and help plan further management of the pregnancy.

For AUB Alumni: AUB "Ob/Gyn Wire"

We proudly announce the recent birth of "Ob/Gyn Wire", a new quarterly newsletter being put forth by the Dept. of Ob/Gyn at AUBMC under the editorial ship of Anwar Nassar, MD. The newsletter is a unique avenue for AUB Ob/Gyn Alumni and friends to stay abreast with the departmental news, on both a professional as well as a social level. It also provides news and updates on AUB Ob/Gyn alumni. Professor Nassar welcomes any interesting announcements and those may be shared with him at an21@aub.edu.lb. For the online access of "Ob/Gyn Wire" please visit: http://satff.aub.edu.lb/~webobs/newsletter.html.

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CFAFC would like to thank Dr. Ahmad El Sheikhah, Dr. Georges Haddad, Dr. Assaad Kesrouani, Dr. Bernard Nasr and Dr. Anwar Nassar for their contributions to this issue. And on February 24, 2012, CFAFC and CFAFC's Newsletter celebrate their 2nd anniversary. As such, we extend our sincerest appreciation to our readership...

CFAFC is now on

For any interesting case reports, comments, suggestions or announcements to be included in our newsletter, please send an e-mail to rar@cfafc.org.

Prenatal Diagnosis Of Fryns Syndrome

By Bernard Nasr, MD

A 32 year old, G2P1, with a negative medical history and a prior obstetrical history notable for a term delivery of a baby with a congenital diaphragmatic hermia (CDH), now presented at 17 weeks for a genetic sonogram. The scan revealed a fetus with an abnormal profile (Figure 1) and multiple anomalies including a CDH (Figures 2,3), Dandy-Walker malformation (Figure 4), ventriculomegaly (Figure 5) and agenesis of the corpus callosum (Figure 6), clinically consistent with Fryns Syndrome. Amniocentesis revealed a normal karyotype, Though two microdeletions have been identified in Fryns syndrome, involving chromosome 15q26.2 and chromosome 8p23, microarray analysis for specific microdeletions is currently not available. The couple elected termination and a postmortem examination was declined.

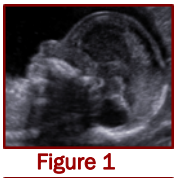
Figure 1

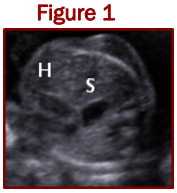

Figure 2

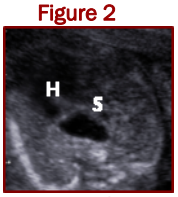

Figure 3

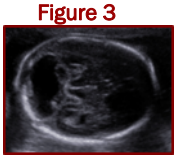
Figure 4

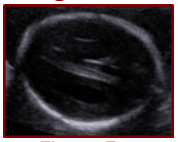
Figure 5

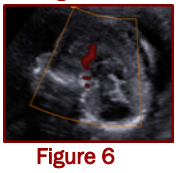
Figure 6

Fryns syndrome was first reported as a lethal condition but 14%, with milder anomalies survive the neonatal period. About 80 cases have been reported in the literature thus far. Today the prenatal diagnosis of Fryns syndrome is feasible, primarily via the ultrasonographic detection of diaphragmatic hernia and cystic hygroma.

Upcoming Congresses

COURSE TITLE	DATES	LOCATION	WEBSITE ADDRESS
Annual Convention of the American Institute of Ultrasound in Medicine	Mar 29-April 1, 2012	Phoenix-AZ, USA	www.aium.org/cme/events/ann2012/ann2012.aspx
Effective Prenatal Screening of Congenital Heart Disease	April 7-9, 2012	London, UK	E-Mail: c.lim@rbht.nhs.uk
Kasr Al Ainy's 13th Annual Congress in Ob/Gyn	April 12-13, 2012	Cairo, Egypt	www.obgynkasralainy.com
Ultrasound 2012	April 12-14, 2012	Boston-MA, USA	www.radcme.harvard.edu/PDF/US_1gpages_2012.pdf
Controversies in Obstetric Doppler	April 14-15, 2012	London, UK	E-Mail: dl342@medschl.cam.ac.uk
Nouvelle Journees d'Echographie Foetale	May 17-20, 2012	Paris, France	www.cfef.org/editorial.php
8th International Symposium of ISUOG	May 31-June 3, 2012	New Delhi, India	www.isuogsymposiumindia.com
16th International Conference of the International Society of Prenatal Diagnosis	June 3-6, 2012	Miami-FI, USA	www.ispdhome.org/conference/2012
Perinatal Medicine 2012	June 13-16, 2012	Paris, France	www.mcaevents.org/ecpm2012/
11th World Congress in Fetal Medicine	June 24-28, 2012	Kos, Greece	www.fetalmedicine.oom/fmf/courses-congress/conferences/