



# Center For Advanced Fetal Care Newsletter

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## INSIDE THIS ISSUE

Unity Is Our Strength	1
FMFA in Spina Bifida	1
Yolk Stalk Sign	1
Synopsis: ISUOG Prague	2
CFAFC Recommends	3
Global Issues	3
Future Trends	3
Recommended Courses	3
Case Report	4
Upcoming Courses	4

## Unity Is Our Strength...

In this day and age, and with the over abundance of medical research and publications, subspecialists become the only avenue towards the mastery of all the corresponding skills and knowledge. Our subspecialists form the pillars in maternal fetal care where the challenging cases require a holistic integrated approach encompassing the expertise of the obstetrician, maternal fetal medicine specialist, geneticist, pediatric cardiologist and pediatric surgeon...Through this coordination of care and the integration of the expertise of those subspecialists, the future shall bear witness to better maternal and fetal outcomes...This issue is dedicated to the 'holistic approach'. We present to you highlights from the International Society of Ultrasound in Ob/Gyn's 20th Annual Congress, an integrated congress uniting obstetricians, gynecologists, fetal medicine specialists, sonologists, radiologists to name a few... A most inspiring futuristic work by Abi-Nader et al is presented addressing a major cause of fetal and neonatal morbidity and mortality, namely intrauterine growth retardation. Here, and through the integration of genetics, virology, as well as maternal fetal medicine, ingenious techniques have been developed that hold great promise for the future of these at risk fetuses. Again, integrating fetal medicine, pathology, laparoscopic surgery as well as the various diagnostic modalities gives birth to Sebire's "Minimally Invasive Autopsy" reviewed in this issue as well. Bianchi et al's 2nd edition of "Fetology" is our chosen literary recommendation for this issue, a gold standard in this integrated holistic approach. In addition, this month's clinical case presentation is a cardiac case in which the prenatal diagnosis and coordination of care between the obstetrician and the pediatric cardiologist altered the outcome for the neonate. Our hope is that this issue clarifies and solidifies our commitment to the integrated approach: unity is our strength, in medicine as in everything else...

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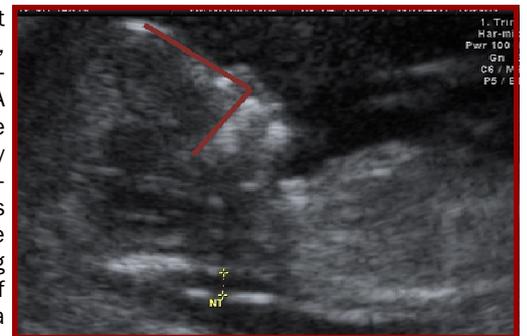
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## Frontomaxillary Facial Angle in Spina Bifida

Ever since Chaoui et al described the intracerebral translucency (IT) a year ago, several studies have been carried out to assess its role in the early detection of spina bifida (SB), as presented at the 20th World Congress of the International Society of Ultrasound in Obstetrics and Gynecology. A new, interesting study by Lachmann et al now looks at the fronto maxillary facial angle (FMFA) and its role in the early detection of SB. This study compared the FMFA in 20 patients with open SB and 100 normal controls. The FMFA was 9.9 degrees less in the open SB group in comparison to the normal controls. The authors thus conclude that measuring the FMFA, in addition to its role in the early detection of trisomies as part of the first trimester scan, may now play a role in the early detection of SB. UOG 2010; 36:268-271.



## Yolk Stalk Sign

It is always challenging when on a first sonographic evaluation, a conclusive diagnosis must be reached of whether one is dealing with a missed abortion or an early IUP with no clear fetal heart tones. The study of Filly et al is a retrospective study that addresses this specific issue and calculates the positive predictive value of the yolk stalk sign. The authors specifically address fetuses of a crown rump length of at least 5 mm without clear cardiac activity. In case the fetus is still in close proximity to the yolk sac, then this is more than likely a very early pregnancy and care must be taken before confirming fetal demise. If on the other hand, the fetus has migrated away from the yolk sac, then irrespective of whether or not the "yolk stalk" is clearly visible, it must have developed, a sign of advanced gestation where clear cardiac activity should have been seen. In these cases, with a fetus of at least 5mm, a yolk stalk sign and no cardiac activity, it is feasible to conclude early fetal demise. The positive predictive value in this study was found to be 100%. Filly et al J Ultrasound Med 2010; 29:237-241.

## Highlights from ISUOG's 20th World Congress on Ultrasound in Obstetrics and Gynecology, Prague, Czech Republic, October 10-14, 2010



Here are highlights from ISUOG's 20th World Congress. The congress was attended by 2000 delegates from over 170 countries with a new congress format and many workshops. The 21st World Congress will be held in Los Angeles, September 2011.

### Cardiac Structures at less than 16 weeks are Enlarged in the Fetus with increased NT. Rychik et al

Even though the pathophysiology of increased 'nuchal' translucency (iNT) remains unknown, Rychik et al compared the size of cardiac structures in fetuses with and without iNT. The 2 groups included only normal fetuses. Those with 'aneuploidy' or congenital heart defects were excluded. There were 35 fetuses with iNT and 76 with normal NT. The groups were comparable in all demographics. Fetuses with iNT had greater diameters for tricuspid and mitral valves and both their ventricles were longer. The authors conclude that the increased circulatory volume in early gestation is what leads to greater growth of those structures and explains the iNT in those fetuses versus the ones with a normal NT.

### Prenasal Thickness is 2/3 of Nasal Bone Length, an Easy to Use Ratio, Significantly Higher in Trisomy 21, in the Second and Third Trimesters. De Jong-Pleij et al

De Jong-Pleij et al determine the stable prenasal thickness (PT) to nasal bone length (NBL) ratio in 100 euploid fetuses to be 2/3 in the second and third trimesters. This ratio remains stable, though significantly higher, when it was evaluated in 26 fetuses affected by trisomy 21 owing to more PT and smaller nasal bones with a mean of 1.57 ( $P < 0.001$ ). The authors thus conclude that with the stability of this PT/NBL, at around 2/3 in euploid and 1.57 in trisomy 21 fetuses, in the second and third trimesters, we may now have a good new sonographic marker for identifying affected fetuses.

### The "Evanescence Pelvic Translucency" a Major Finding of Anal Atresia in the First Trimester. Bault et al

The role of the first trimester scan is further expanding in the early diagnosis of structural anomalies. This is further exemplified by the work of Bault et al who describe a new first trimester marker 'evanescent pelvic translucency' in the early diagnosis of anal atresia. They report on 5 cases presenting with an abnormal ellipsoid echogenicity pelvic translucency before 14 weeks that disappears beyond the first trimester. In 3/5 cases, anal atresia was confirmed at birth. Two elected to terminate and pathology was available on one of those cases and confirmed the diagnosis. The authors interpret this finding to be a result of a fistula between the bladder or uretra with the intestinal tract. It disappears with the accumulation of meconium within it. Such a finding should lead to early first trimester suspicion of anal atresia and subsequent confirmation in the second trimester by demonstrating the absence of the lower part of the rectum.

### Increased NT and Normal Karyotype: Perinatal and Pediatric Outcome at 2 Years of Age. Mula et al.

Mula et al tackle the big question of 'what after an increased nuchal translucency and normal karyotype?' by providing perinatal and pediatric outcome at 2 years of age. They followed 171 singletons with NT  $> 99\%$ . Of those, 7 were fetal demises, 2 postnatal deaths and 38 terminations. Among the remaining 124, 112 (66%) were born without any defects. On those 112, 86% had neurodevelopmental followup and 6% were abnormal. The authors conclude that in fetuses with NT  $> 99\%$  there is a 73% survival, of those 10% had structural anomalies and 6% neurodevelopmental abnormalities.

### Fetal Isolated Ventriculomegaly: Results of a Longterm Prospective Prenatal/Postnatal Cohort. Bello-Munoz et al

Bello-Munoz evaluate 45 fetuses referred for isolated ventriculomegaly. Of those, 60% were mild ( $< 12$  mm), 7% moderate (12-15 mm) and 33% severe ( $> 15$  mm). Follow up included MRI at 26-30 weeks, and postnatal followup using PEDS test till a maximum of 5 years of age. The authors conclude that truly isolated ventriculomegaly had good long term prognosis and that all possible measures, such as fetal MRI, should be utilized to rule out the association with any further CNS anomalies.

### Identification of Fetal Abnormalities in the Third Trimester After a Second Trimester Detailed Structural Fetal Survey. Shipp et al

Shipp et al address the rule of third trimester ultrasound in the denovo diagnosis of structural abnormalities after a normal second trimester scan. Here the authors evaluate 4170 fetus in the third trimester. In 98 (2.4%), there was the new identification of previously undetected structural anomalies. Renal (primarily hydronephrosis) constituted 72.4%, however postnatally, 96.6% were not found to have hydronephrosis at birth. Other abnormalities included the CVS 0.2%, vascular abnormalities 0.1%, GI 0.1%, neurological 0.1% and face 0.1%. The authors conclude that though a third trimester scan may detect new anomalies, the majority are renal with normal neonate. They thus call to the reevaluation of third trimester thresholds for hydronephrosis.

Proceedings are available in the society's journal: *Ultrasound in Obstetrics & Gynecology*, Volume 36, Supp 1, October 2010. Taped congress sessions are available on the Society's website at: [www.isuog.org](http://www.isuog.org)

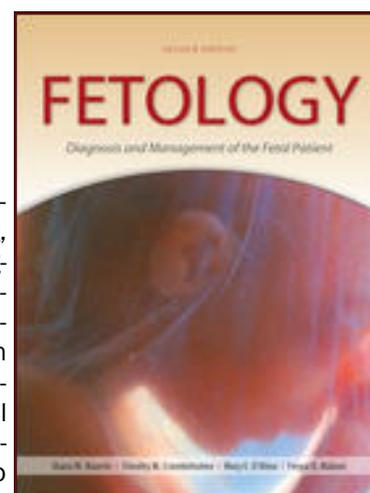
## CF AFC's Literary Recommendation

### Fetology: Diagnosis and Management of the Fetal Patient

Authors: Diana Bianchi, Timothy Crombleholme, Mary D'Alton and Fergal Malone

Publisher: Mc-Graw-Hill Professional, 2nd Edition, 1024 pages, ISBN-10:0071442014, \$165

This second edition of a reference in fetal medicine brings with it a multidisciplinary management approach to obstetrical and fetal care where from an abnormal sonographic finding, genetic result or an abnormality in fetal growth further management is recommended: pregnancy management, newborn therapy, or any additional genetic testing etc...It is a unique multidisciplinary approach combing the expertise of a geneticist, a maternal fetal medicine specialist as well as a pediatric surgeon. The text is organized into 3 sections starting with part I in which a comprehensive overview of fetal medicine is carried out. Part II addresses management of fetal conditions diagnosed by sonography and part III addresses management of fetal chromosome abnormalities. This invaluable up-to-date reference is a must have guide especially in non-tertiary care centers where the various experts may not be readily available to further guide the family and plan the rest of the antepartum, peripartum and postpartum care.



## THIS AND THAT

### ISUOG Fetal Echo and Doppler Course

Professor Chaoui's annual ISUOG course on Congenital Anomalies and Fetal Echocardiography is scheduled for Feb 19 and 20, 2011, London, United Kingdom. Course registration and further details may be found at the ISUOG website at: <http://www.isuog.org/FutureMeetingsAndCourses/ISUOG+Organized+courses/>

### ISUOG Outreach: Update

A most inspiring successful workshop was held at the 20th Congress of ISUOG. Members were brought up to date on the Outreach activities in Haiti and Ghana with much expansion planned for the coming year. For more information, you may watch the free web lecture by Professor Abuhamad, the chairman of ISUOG's Outreach committee, entitled: Maternal Mortality: A Global Crisis, Is There A Role For Ultrasound? The link to this webcast is:

[http://isuogonline.insync.com/Congress/Hamburg2009/Plenary/Abuhamad\\_Outreach\\_weblecture/index.html](http://isuogonline.insync.com/Congress/Hamburg2009/Plenary/Abuhamad_Outreach_weblecture/index.html)



ISUOG Volunteers, Ghana Sept 2010 (L to R): D. Paladini, A. Abuhamad, S. Horton, L. Hanson, B. Del Prince and A. Tabor

### Minimally Invasive Autopsy

Fetal autopsy is under-utilized for several reasons, at the forefront of which is the parents' wishes to leave their baby intact. This limits the expertise needed in this most important field and hinders achieving an accurate diagnosis at many centers, with limited numbers of annual fetal autopsies. However, under the guidance of Dr. Sebire and his futuristic trends, we have a novel integrated approach combining his profound knowledge of fetal medicine, pathology and the various diagnostic modalities. As a result, we now have the emergence of the "minimally invasive autopsy" which uses the laparoscopic approach as well as several other diagnostic modalities, leaving minimal fetal marks and gaining more and more acceptance. A web-based lecture is available free of charge at:

<https://courses.fetalmedicine.com/videos/lectures/lecture.html?file=sebire2.flv>

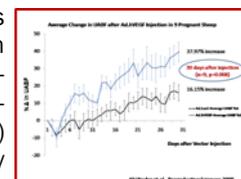
### Gene Therapy for Placental Insufficiency

K. Abi-Nader, MD & A. Davis, PhD

Placental insufficiency affects up to 10% of pregnant women. It usually presents as intrauterine growth-restriction, pre-eclampsia, or a combination of both. When the condition occurs early in pregnancy, the placental dysfunction is usually so severe that it compromises the ability of the fetus to reach a viable birthweight to survive.

A common final pathway in placental insufficiency is impaired utero-placental perfusion which is reflected in a decreased uterine artery blood flow (UABF). UABF is directly proportional to fetal size in sheep and in women with growth-restricted fetuses, it is reduced (Lang et.al. 2000, Konje et.al. 2003). Placental insufficiency has no effective treatment. We thought that local over-expression of vascular endothelial growth factor (VEGF) in the uterine arteries (UtA) will increase utero-placental perfusion through vasodilation and neovascularization (David et.al. 2008). In our latest experiments we show that an adenovirus (Ad) carrying the human VEGF gene can safely sustain a long-term increase in UABF (Abi Nader et.al. SGI Abstract 2009).

Transit-time flow probes (Transonic Inc, USA) were implanted around both uterine arteries of mid-gestation pregnant sheep (n=9, 90 days of gestation, term=145 days) and UABF was measured via telemetry (Figure 1). A carotid artery catheter was inserted to measure maternal (n=4) or fetal (n=4) hemodynamics through open fetal surgical techniques. Baseline UABF was measured prior to injection of Ad.VEGF-A<sup>165</sup> into the UtA on one side and a reporter gene (Ad.lacZ) into the contralateral side. UABF was then measured daily until term. UABF significantly increased from baseline in Ad.VEGF-A<sup>165</sup> compared to Ad.lacZ transduced UtA and the increase was sustained for at least 4 weeks (37.97% vs 16.15%, p=0.008, Figure 2). There was no significant short or long term effect on maternal and fetal hemodynamics. At the same time, the treatment appears to be safe which makes clinical application a true possibility.





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CFAFC would like to thank Drs. Abi-Nader and Daou for their contributions to this issue.



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**Case Report: Late Third Trimester Prenatal Diagnosis and Management of Fetal Aortic Coarctation by R. Abu-Rustum and L. Daou**

A 31 yo MWF G3 P1011 with good prenatal care, an NT of 1.8mm at 13w2d and a normal second trimester scan except for a perimembranous VSD, was undergoing third trimester scan at 34w1d. It was noted that the left ventricle was smaller than the right and the 3 vessel trachea view revealed an aorta that is smaller than the pulmonary artery. Further investigation of the aortic arch on sagittal views, with and without color Doppler, clarified a contraductal shelf and aortic coarctation. Pediatric cardiology confirmed the diagnosis and the decision was made to deliver this baby at a University Center with a well equipped pediatric cardiology unit. A live-born female was delivered at 38 weeks. Postnatally the diagnosis was confirmed and the baby underwent postnatal surgery. She is alive and well at 1 year of age now. This integrated approach ensured the best possible outcome for this baby, sparing her any hypoxia that would have resulted from delay in diagnosis and transfer if this diagnosis had been missed antenatally...



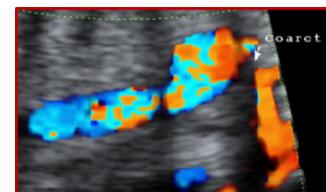
Ventricles: L<R



With color Doppler



Contraductal shelf



Contraductal shelf with and without color Doppler

**Upcoming Congresses**

COURSE TITLE	DATES	LOCATION	WEBSITE ADDRESS
Fetal Medicine Foundation's Advanced Ultrasound Course	November 6-7, 2010	London, UK	www.fetalmedicine.com/fmf/courses-congress/03-fmf-courses/
Obstetrical Ultrasound in the High Risk Patient	November 12-14, 2010	Las Vegas, Nevada	www.iame.com
Intensive Fetal Cardiology Course	November 13-14, 2010	London, UK	www.ichevents.com
13th Annual Mid-Atlantic Ultrasound Symposium in Ob/Gyn	November 19-20, 2010	Virginia Beach, Virginia	http://cmetracker.net/EVMSCME/Files/Brochures/15971.pdf
19th Annual Ob/Gyn Update for Clinical Practice	December 2-5, 2010	Fort Lauderdale, Florida	www.cmebyplaza.com/Registrants/GoHo10/About.aspx
31 Annual Meeting of the Society of Maternal Fetal Medicine	February 7-12, 2011	San Francisco, California	www.smfm.org/Annual%20Meeting%20Page.cfm?ht=me
Congenital Anomalies and Fetal Echocardiography	February 18-19, 2010	London, United Kingdom	www.isuog.org/FutureMeetingsAndCourses/ISUOG+Organised+courses/
14th Annual Obstetric Ultrasound	March 4-6, 2011	Toronto, Canada	www.mountsinai.on.ca/education/staff-professionals/cme
Annual Convention of the American Institute of Ultrasound in Medicine	April 14-17, 2010	New York, USA	www.aium.org