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## 1095-201 QRS Duration and Depolarization Heterogeneity in Tetralogy of Fallot Patients Before and After Surgical Repair of the Pulmonary Valve

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**Background.** QRS duration has a strong predictive value in Tetralogy of Fallot (ToF) patients, and is associated with arrhythmic death. One possible mechanism for increased arrhythmia vulnerability is that prolonged QRS duration contributes to repolarization heterogeneity. A positive association between QRS duration and QT dispersion has been reported in ToF patients, however, it is generally recognized that QT dispersion is unlikely to reflect repolarization heterogeneity. Here we investigate, in ToF patients, the relation between QRS duration and the second component of the singular value decomposition (SVD) of the T wave, which is mathematically related to repolarization heterogeneity (Van Oosterom, Int J Bioelectromagnetism 2002; 4: 59-60).
**Methods.** We analyzed two sets of ECGs of 23 ToF patients (13/10 M/F) recorded before and one year after pulmonary valve replacement (PVR) at age 31±8 years. QRS duration was measured by an interactive computer program (Intraval, author HRvE). The second component of the SVD of the T wave was measured by a Matlab program (authors CAS, HvdV, ACM).
**Results.** QRS duration after PVR (143 ± 31 ms) was significantly smaller than before PVR (148 ± 31 ms, $P<0.01$). The second SVD component of the T wave after PVR (134 ± 71 μV) was significantly smaller than before PVR (164 ± 93 μV, $P<0.05$). QRS duration correlated significantly with SVD before PVR ($r=0.48$, $P<0.05$) and after PVR ($r=0.43$, $P<0.05$).
**Conclusions.** QRS duration in ToF patients correlates significantly with the second SVD component of the T wave, before and after PVR. This finding suggests that impaired intraventricular conduction (expressed in QRS duration) in these patients causes part of the impaired repolarization heterogeneity (expressed in the second SVD component of the T wave), thus contributing to increased risk of arrhythmogenic death. PVR may reduce arrhythmia vulnerability by diminishing repolarization heterogeneity.

## 1095-202 Can We Predict Sudden Death After Atrial Repair for Transposition of the Great Arteries?

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**Background**: Sudden death (SD) is the commonest cause of late death in patients who undergo atrial repair of transposition (TGA) by Mustard's/Senning's technique. Little is known about the predictors of SD.
**Methods**: We performed a retrospective, multi-center, case-controlled study. TGA patients (n=47) who had a SD event (34 SD, 13 near miss SD) were matched (except one patient (who had only one control)) with two controls with TGA but without a SD event from the same center, era and age at surgery. Clinical reports, ECGs, echocardiograms, chest Xrays, Holter monitors, exercise tests, cardiac catheterization reports and electrophysiology (EP) studies were reviewed and compared with same information from controls at the same time frame.
**Results**: Presence of symptoms (of arrhythmia or heart failure) at most recent follow-up and history of documented arrhythmia (supraventricular tachycardia (SVT) in particular) were found to increase the risk of SD. QRS duration, QT and QTc on ECG were not predictive of SD. Neither sinus node dysfunction on Holter nor cardiomegaly on chest Xray were predictive of SD. There was inadequate data on echo, exercise testing, cardiac catheterization and EP findings for meaningful analysis. Neither medication use (mostly digoxin) nor pacing was found to be protective.
**Conclusions**: Presence of symptoms and documented SVT are the best predictors of SD in TGA patients. Patients with these features should be considered high risk and need close follow-up. Aggressive attempts to control SVT using techniques such as catheter ablation are justified in an attempt to prevent SD in these patients.

## 1095-203 Responsiveness to Inhaled Nitric Oxide Is Related to Mid-Term Survival in Patients With Congenital Heart Disease and Obstructive Pulmonary Hypertension

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Background: It was previously demonstrated that in several adults with congenital heart disease and obstructive pulmonary hypertension and/or the Eisenmenger syndrome, the pulmonary circulation remained responsive to inhaled nitric oxide (iNO). The purpose of our study was to evaluate whether the responsiveness to iNO could predict the mid-term outcome of these patients.
Methods: In 21 consecutive patients, the total pulmonary vascular resistance (TPR) was measured at baseline, after 5 minutes inhalation of NO (80 ppm), and after NO withdrawal. Patients were considered responders when TPR was reduced by at least 20 percent during NO inhalation or when TPR increased by more than 10 percent after NO withdrawal. This group of patients was followed prospectively and the primary endpoint of the study was defined as cardiopulmonary death. Kaplan Meier survival curves for responders and the non-responders were plotted and compared by using log rank testing. Statistical significance was defined as $P<0.05$.
Results: Ten patients were considered responders (4 male and 6 female, mean age 35.1 ± 22.7 years). Eleven patients did not respond (2 male and 9 female, mean age 32.7 ± 19.1 years). The median follow up time of the total group was 9.0 years, range 10.2 years. Four of the non-responders died during follow up (cardiovascular death); no events were found in the group of responders. The difference in survival between the responders and non-responders was statistically significant (log rank $P<0.05$).
Conclusions: The responsiveness to inhaled NO in adult patients with obstructive pulmonary hypertension or the Eisenmenger syndrome seems to be related to the mid-term outcome. These findings might be important issue for risk stratification and choice of treatment in this specific patient population.

## 1095-204 Ebstein's Anomaly: Incidence of Left Ventricular Noncompaction

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BACKGROUND Left ventricular noncompaction (NC) has been observed as an isolated anomaly or rarely in conjunction with congenital heart disease involving right or left ventricular outflow tract obstruction. In Ebstein's anomaly (EA), left ventricular anomalies resembling NC have recently been described in 3 of our patients (pt). The aim of the present study was to examine the incidence of left ventricular NC in pt with EA. - METHODS Between July 2001 and Feb 2003, 106 pt [64 females (60 %)], with EA underwent echocardiography at our institution. Data from all charts were collected. Videotapes of all pt were blindly reviewed by at least 2 reviewers looking for NC and other left-sided anomalies. RESULTS Mean age was 32±20 years, 31 pt (29 %) were <18 years at the time of index echo. In 84 pt, there was a history of atrial septal defect (ASD) or patent foramen ovale. A history of previous heart surgery was present in 57 pt (54 %) including 30 pt with tricuspid valve (TV) replacement, 16 pt with previous TV repair and/or 34 pt with closure of an ASD. Symptoms were present in 88 pt (83%), 19 pt (18%) were in NYHA class III or IV at the time of the index echo. Severe anatomic form of EA was described in 76 pt (72 %). The criteria of left ventricular NC were fulfilled in 19 EA pt (18 %). Additional findings included a bicuspid aortic valve in 7 pt (7 %), a ventricular septal defect (VSD) in 8 pt (8 %) and mitral valve prolapse in 16 pt (15 %).
Left ventricular ejection fraction was diminished in 7 pt (7 %), left ventricular dilation was found in 4 pt (4 %). Diastolic dysfunction was present in 34 of 95 pt (36 %). Accessory conduction pathways were present in 23 pt (22 %). The presence of left ventricular NC could not be predicted by any associated anomaly, but tended to be more common in pt with accessory conduction pathways ($p=0.11$).- CONCLUSIONS Anomalies of the left ventricle resembling left ventricular NC is noted in a high percentage of patients with EA (18 %). In addition, ventricular septal defect (8 %) and a bicuspid aortic valve (7 %) are observed in EA with increased frequency compared to non-EA patients. Careful assessment of the left-sided cardiac structures in patients with EA is important as cardiac anomalies are not confined to the right side of the heart.

## 1095-205 Factors Affecting Re-Replacement of the Pulmonary Valve in Children

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Background: Pulmonary valve failure (PVF) in children after pulmonary valve replacement (PVR) is a complex, multi -factorial process. Risk factors for PVF in children have not been systematically defined. If these are identified, this would translate into improved clinical outcomes.
Methods: An IRB approved chart reviewof children with congenital heart disease requiring PVR from January 1987-June 2003 was undertaken using our surgical database. PVF was defined as repeat replacement for valve dysfunction. Time to PVF was determined using actuarial methods. Variables analyzed included patient gender, initial diagnosis, age at surgery, type and size of valve, implantation time, and reason for reoperation. The type and size of second valve were also compared between patients with and without valve failure. Risk factors for failure were sought using univariate and multivariate analysis.
Results: A total of 127 patients underwent PVR, with a mean age of 15.6 +/- 9.3 years. There were 71% patients with TOF type anatomy and 29% with isolated pulmonary stenosis. Pulmonary valve insufficiency was the reason for reoperation in 79% and severe pulmonary stenosis in 21%. Fifty patients (39%) received a cryopreserved pulmonary homograft, 45 (36%) a Hancock porcine and 32 (25%) a Carpentier–Edwards pericardial bioprosthesis. PVF occurred in 19 (15%) patients. At 5 years follow up, PVF rate was 10 % for homografts vs. 10 % in bioprosthetic valves. However at 10 years follow up, 68 % of heterografts failed whereas only 28% of homografts failed. This was statistically significant ($p=0.04$). At 10 years follow up younger age, longer duration of hospital stay and use of bioprosthetic valves were all significantly associated with an increased risk of failure. When homograft vs bioprosthetic valve patient variables were analyzed, there was no difference in patient age, diagnosis, or reason for reoperation.
Conclusion: This is the first study in children which demonstrates that cryopreserved pulmonary homografts have improved durability in the pulmonary position when compared with bioprosthetic valves. It would thus appear to be prudent to preferentially use a cryopreserved homograft in the pulmonary position.

## 1095-206 Pregnancy in Women With Corrected Tetralogy of Fallot

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**Background:** Limited data are available regarding the potential complications of pregnancy, fertility and recurrence risk in corrected Tetralogy of Fallot (ToF) patients. We report the largest study so far.
**Methods:** In this multicenter study 79 patients with corrected ToF were enrolled. For all patients information regarding fertility and cardiologist's advise about pregnancy was obtained. For each pregnancy detailed information about haemodynamics, ultrasound, obstetric status, delivery and pediatric examination was collected. Questionnaires were

used to supplement the information available from the medical records.
**Results**: 3 patients were pregnant (for the first time) at enrollment, 54 patients were childless. 46 pregnancies, which resulted in live birth, were observed in the remaining 22 patients. In addition, 2 abortions (1 elective) were reported in the childless group and 10 (0 elective) in the patients with children. Mean age of the childless patients was 26 (SD 5,74), in patients with children 34 (SD 5,78) years. 5 patients reported fertility problems and only 1 patient was advised against pregnancy by her cardiologist. Maternal complications were: arrhythmia (n=6) and heart failure (n=2), in 5 patients and in 6 pregnancies. Caesarian section was performed 13 times (28%), of which 5 on maternal cardiac indication. Mean birth weight was 3064 g (SD 728). 5 births were premature (between 16 and 37 weeks) and 8 children (17%) were small for gestational age (<p10). 3 children died within the first year of life. 2 children (4,3%) had congenital heart disease: 1 child had ToF (died at 10 months), the other had several cardiac malformations in combination with trisomie 13.
**Conclusion**: In patients with ToF pregnancy is generally well tolerated. However, maternal cardiac complications do occur in 13% of pregnancies. The need for Caesarian section was increased. The incidence of small for gestational age children was increased. Fertility seems not to be compromised.

POSTER SESSION

## 1114 Pediatric and Congenital Heart Disease

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

### 1114-198 Genomic Profiles of Left Ventricular and Right Ventricular Hypertrophy in Congenital Heart Disease

Beth D. Kaufman, Juan C. Osorio, Manisha Desai, Jonathan Chen, Ralph S. Mosca, Jan M. Quaegebeur, Anthony W. Ferrante, Seema Mital, Columbia University, College of Physicians & Surgeons, New York, NY

**Background:** Hemodynamic stimuli promote activation of gene expression pathways that mediate ventricular hypertrophy. The LV has a greater ability to tolerate hemodynamic load than the RV. Regulation of this differential response is not known.
**Methods:** Hypertrophied myocardium was obtained at surgery from 9 acyanotic pediatric pts, 4 LVH and 5 RVH (age 0.15-6.7 yrs). Diagnoses included subaortic stenosis, subpulmonary stenosis, and hypertrophic cardiomyopathy. Gene expression (GE) with Affymetrix DNA microarray gene chips was performed. After log transformation, differences in mean GE between LVH and RVH groups with p value <0.01 was considered significant. Genes with > 2-fold difference between the 2 groups were characterized and correlated with severity of obstruction. Immunohistochemical staining was performed to detect myocyte apoptosis with TUNEL assay, and fibrosis with trichrome stain in myocardium from 10pts with LVH and/or RVH.
**Results:** There were 253 genes with significant differences in expression between LVH and RVH myocardium samples. 124 genes associated with myocardial hypertrophy, cytoskeleton, apoptosis, and ion channels were upregulated in LVH. RVH group had 129 genes relatively overexpressed: extracellular matrix components, phospholipase A2 and C, and mitochondrial transporter proteins. Fetal gene activation was present in both LVH and RVH, with relative overexpression of cANF and dystrophin in the LV compared to RV (p values <.01). Severity of obstructive gradients in both groups correlated positively with actin and myosin GE, and negatively with apoptosis related genes (r = 0.8-0.9). ANP GE correlated with LV obstruction only. Fibrosis and myocyte apoptosis was present in both LVH and RVH specimens, but was greater in pts with HCM than those with isolated outflow tract lesions.
**Conclusion:** Myocardium from hypertrophied LV and RV has different genomic profiles. Upregulation of genes in the LVH group that activate adaptive pathways may contribute to the functional advantage observed in the LV vs. the RV with hemodynamic load, especially in pts with congenital heart disease. Further analysis of these candidate genes and downstream signaling effects are warranted.

### 1114-199 A Comparison of Postnatal Changes in Fetal Phenotype Between the Left and Right Ventricles

Ana M. Duque Gonzalez, Juan C. Osorio, Susan Vannucci, Seema Mital, Columbia University, New York, NY

**Background:** The transition from fetal to neonatal circulation is characterized by an increase in LV and decrease in RV size and thickness. This is associated with the disappearance of fetal genes and expression of adult genes in the LV. The role of these adaptive genes in mediating RV remodeling has not been studied. The objective was to determine the pattern of activation of fetal proteins in the left and right ventricles after birth.
**Methods:** Hearts from 2 and 8 days old neonatal Sprague-Dawley rats (n=6 litters) were isolated. In a novel approach, LV and RV were separated and expression of fetal proteins was measured using Western blots - $\alpha$ -myosin heavy chain (MHC), $\alpha$ sarcomeric actin, c-myc, c-jun (proto-oncogenes), atrial natriuretic peptide (ANP), and Glut 1 (glucose transporter). The expression of upstream signaling proteins - protein kinase B (Akt), and total and phosphorylated mitogen-activated protein kinases (MAPK – JNK, P38 MAPK, p44/42) were also compared between LV and RV.
**Results:** At 2 days, the expression of $\alpha$ -MHC, ANP, Glut 1, ph-Akt, ph-JNK, and ph-p44/42 were 20-70% lower in RV compared to LV (p<0.05). c-myc expression was not different between LV and RV. ANP, c-myc, ph-JNK and ph-p44/42 increased in the LV at 8 days. In contrast, the RV showed a decrease in ANP and no change in c-myc despite an increase in ph-JNK and ph-p44/42. Of the cytoskeletal fetal proteins, actin was higher in the LV and $\alpha$ -MHC was higher in the RV at 8 days. Glut-1 was lower in RV at birth but increased to levels seen in LV by 8 days.
**Conclusions:** Fetal proteins are down-regulated in the RV compared to the LV at birth, including cytoskeletal, metabolic and immediate early genes. This may be related to decreased activation of MAPKs and Akt in the RV and may account for decreased RV growth post-natally. Whether the lower adaptibility of the RV compared to the LV to hemodynamic load in disease is related to a reduced ability to activate or reactivate fetal genes requires further study. To our knowledge, this is the first report comparing adaptive pathways between the LV and RV. Knowledge of these differences will be important in individualizing therapy to the pathways specific to each ventricle.

### 1114-200 Increased Incidence of Pulmonary Vein Stenosis in Patients With Atrioventricular Canal: A Multi-Institutional Study

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**Background:** Patients with atrioventricular canal (AVC) appear to be at greater risk for the development of elevated pulmonary vascular resistance (PVR) than patients with other cardiac defects. Review of our experience at a single institution suggested the incidence of pulmonary vein stenosis (PVS) may be greater in a subgroup of patients with AVC than in patients with other lesions. We set out to determine if this pattern held true in a larger patient population.
**Methods:** The Pediatric Cardiac Care Consortium data base from 1981 to 2001 (n=90,879) was searched for all patients with a diagnosis of pulmonary vein obstruction (PVS or cor triatriatum) and yielded 840 (0.9%) patients. Analysis by chi square was performed on a subset of patients excluding those with a diagnosis of anomalous pulmonary venous connections and a subset excluding those with a diagnosis of anomalous pulmonary venous connections or cor triatriatum. The relationship of Trisomy 21 with pulmonary vein obstruction was also investigated.
**Results:** After excluding cases with anomalous pulmonary venous connections, 509 (0.9%) patients were identified with pulmonary vein obstruction. In this group, 280 (0.3%) patients were identified with PVS by excluding those with a diagnosis of cor triatriatum. AVC was found with greater frequency in subsets of patients with pulmonary vein obstruction, 13.7% (70 of 509, p<0.00001) and PVS, 12.5% (35 of 280, p=0.0028) as compared with an 8.4% prevalence of AVC in patients without pulmonary vein obstruction (6,661 of 79,656, excluding anomalous pulmonary venous connections). There was no association of Trisomy 21 with pulmonary vein obstruction (p=0.4).
**Conclusion:** Patients with AVC are at greater risk for concomitant pulmonary vein obstruction and PVS than are patients with other congenital cardiac defects. Patients with AVC and evidence of elevated PVR should undergo careful scrutiny of pulmonary venous connections either by echocardiography or cardiac catheterization. Trisomy 21 does not appear to be associated with the increased incidence of pulmonary vein obstruction.

### 1114-201 Higher Mortality After Fontan Surgery in Trisomy 21 Syndrome Children

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**Background:** High pulmonary artery pressure (PAP) is associated with increased mortality after Fontan surgery. It is not known whether Trisomy 21 syndrome patients have a higher PAP prior to Fontan when compared the to the non-Trisomy 21 patients.
**Methods:** We retrospectively evaluated data from our Pediatric Cardiac Care Consortium (a data bank for all cardiac surgery cases from participating centers). Of the total Fontan surgeries (n = 1966), 17 were performed on Trisomy 21 patients (Group II). Group I were non-Trisomy patients after Fontan (n = 1949). Of Group II patients, 13 patients (Group III) had had Fontan for unbalanced atrioventricular canal defects. Since it would difficult to go through charts of such a large population, we selected a control group from the Group I a total of 28 patients (Group IV) with atrioventricular canal defect who were age (at Fontan) and sex matched and who were alive after the surgery. We evaluated the pre-Fontan mean PAP in mmHg, pulmonary vascular resistance in woods units (PVR), length of stay in days at hospital after surgery (LOS), weight in Kg at surgery (WT), Hemoglobin prior to surgery in g/dL (Hb), whether there was prior Glenn surgery or not, whether the Fontan was fenestrated (FEN) or not and whether there was preoperative atrioventricular regurgitation (AVVR) or not.
**Results:** Between Groups I and II there was significantly higher mortality (p = 0.001)) in Group II (n = 6/17, mean age at surgery 4.8 years) as compared to Group I (n = 204/1949, mean age at surgery 6.6 years) without significant difference between the age, Hb, WT and LOS. Between Group III (WT 16.2, Glenn 85%, AVVR 62%, FEN 54%, PAP 13.8, PVR 2.9, Hb 15.9, LOS 21) and Group IV (WT 22, Glenn 61%, AVVR 57%, FEN 29%, PAP 12.9, PVR 2.9, Hb 15.7, LOS 14) there were no significant differences in the parameters evaluated. Hence, in the selected population of Trisomy 21 who underwent Fontan surgery, PAP and PVR were similar to the non-Trisomy 21 children.
**Conclusion:** The PAP is similar between Trisomy and non-Trisomy patients prior to Fontan. Trisomy 21 syndrome is an independent parameter associated with significantly higher risk of mortality (35%) after Fontan surgery as compared to non-Trisomy 21 patients (10%).