subgroups. Participants completed validated, age-appropriate questionnaires examining standard psychological parameters. Participants also underwent an evaluation of exercise, including formal exercise stress testing and measurement of free-living activity using an ActiGraph accelerometer. Results were analysed using parametric methods. 143 patients (mean age 15.6 years) consented to participate, 86 were male (60%) and 105 had major CHD (73%). Diagnostic subgroups included 39 acyanotic (27.3%), 61 acyanotic corrected (42.7%), 30 cyanotic corrected (21.0%) and 13 (9%) cyanotic palliated patients. Beck Youth Inventory demonstrated that individuals with major CHD, particularly cyanotic palliated patients, had higher anxiety scores (p value 0.01 (−8.42, −1.13)). There were no significant differences across study groups for self-esteem or other psychological parameters. 134 participants (93.7%) took part in regular exercise each week. There was no significant difference in activity score between study groups. On formal exercise testing, more complex patients performed worse at peak exercise. Exercise time for acyanotic group 11.73 mins (sd 3.74) compared to 8.26 mins (sd 4.08) in cyanotic palliated group, p value 0.002 (1.32, 5.61)). However, patients with major CHD had significantly higher activity counts. Correlation analysis showed that self-esteem and health locus of control were important predictor variables for activity. Self-esteem and mood seem well preserved in adolescents with CHD as a whole. The majority of young people with CHD, in this group, take part in regular exercise. Surprisingly, complex patients rate themselves to be as active as those with minor CHD. While accelerometer data indicate that the group may be more active day to day, they are limited in terms of peak exercise duration. The experience of growing up with a chronic condition may therefore have a positive effect on psychological health and interventions targeted around this area may influence activity.

134 MUTATIONS IN THE SARCOMERE PROTEIN GENE MYH7 IN EBSTEIN'S ANOMALY

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Background Ebstein's anomaly is a rare congenital heart malformation characterised by adherence of the septal and posterior leaflets of the tricuspid valve to the underlying myocardium. As there have been reports of abnormal left ventricular morphology and function in patients with Ebstein's anomaly we hypothesised that mutations in the β-myosin heavy chain (MYH7) may be associated with Ebstein's anomaly.
Methods MYH7 mutation analysis was undertaken in 141 unrelated affected individuals with Ebstein's anomaly using next-generation sequencing on the 454 platform. 64 probands had no associated cardiac anomalies. The most common associated cardiac malformation were atrial septal defect (48 probands) and left ventricular non-compaction (LVNC) (7 probands). Where mutations were discovered, family studies were undertaken and the segregation of the mutation with disease was investigated.
Results Heterozygous mutations were identified in eight of the probands including six of the seven with LVNC. Two patients had the same mutation; of the seven distinct mutations, five were novel (four missense changes and an in-frame deletion) and two have been previously reported in patients with hypertrophic cardiomyopathy. Family studies revealed additional members with LVNC for three of the probands, one of whom also had a relative with Ebstein's anomaly. In these three pedigrees the mutation segregated with disease.
Conclusions Mutations in MYH7 occur relatively frequently in Ebstein's anomaly accompanied by LVNC. This study is another example of mutations in a sarcomere protein causing congenital heart malformation.

135 GENE SCREENING OF THE SECONDARY HEART FIELD NETWORK IN TETRALOGY OF FALLOT PATIENTS

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Background Tetralogy of Fallot (TOF) is the most common cyanotic heart defect, affecting 3–6 infants for every 10 000 births. TOF is phenotypically well defined; it consists of four heart abnormalities: a VSD, an over-riding aorta, a narrowed pulmonary valve and right ventricular hypertrophy. During heart development two heart fields can be distinguished. The first one gives origin to the left ventricle and contributes to the right and left atria. The secondary heart field gives origin to the right ventricle and the outflow tract. Each of these fields can be identified by the expression of specific markers. As TOF is a malformation of the outflow tract, we hypothesised genes involved in the regulatory network of the secondary heart field were particularly good candidates for TOF susceptibility.
Methods We examined by standard Sanger method the full exonic and intron boundary regions of 14 secondary heart field genes, namely *NKX2-5, GATA4, TBX20, MEF2C, BOP, HAND2, FOXC1, FOXC2, TBX1, FOXA2, FGF10, FGF8, ISL1* and *FOXH1*, in a panel of 93 TOF patients. All newly discovered rare variants were checked in a panel of 1000 control chromosomes by multiplex Sequenom assays. When available, parents of cases were screened to assess inheritance of the rare variant.
Results We re-sequenced a total of 80 exons and ~30 Kb. Among the 14 genes studied we found a total of 50 new variants, of which 23 were exclusive to the patient population, ie, were absent from 1000 normal chromosomes. Nine of these variants cause change in the aminoacid sequence. We found a functional 19aa deletion of a highly conserved region of *TBX1*. In *FOXC1* we found a contraction of both alanine and glycine tracts. An alanine expansion, usually known to be deleterious, was found in *HAND2*. Four non-synonymous changes were found in *FOXA2*. Most patients presented just one variant, however 3 patients presented two, and one patient presented up to 3 variants. All patients were heterozygotes for the variants, and had inherited them from one of their phenotypically normal parents (when parental information was available). In addition, 75% of the variants were inherited from the mother.
Conclusions Although genes of the secondary heart field seemed good candidates for TOF susceptibility, thus far we have not found any strong indication of unique causal effect, as all variation found in probands was also present in their unaffected parents. However, the presence of multiple variants in the same proband may result in the disruption of gene-gene interactions in the secondary heart field pathway, which in turn may lead to outflow tract defects. Based on our results, it would seem more likely that susceptibility to TOF be determined by a larger number of small genetic contributions which are also modified by environmental factors. It is evident that larger scale analysis of significant numbers of whole genomes/exomes will be necessary to better understand the molecular aetiology of TOF.

136 SHOULD FAMILIAL SCREENING BE ROUTINELY OFFERED TO PATIENTS WITH BICUSPID AORTIC VALVE DISEASE?

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Background Bicuspid aortic valve (BAV) disease is one of the most common congenital cardiac abnormalities with prevalence in the