Population-based evaluation of a suggested anatomic and clinical classification of congenital heart defects based on the International Paediatric and Congenital Cardiac Code

Lucile Houyel [Orateur] (1), Babak Khoshsood (2), Robert H. Anderson (3), Nathalie Lelong (2), Anne-Claire Thieulin (2), François Goffinet (2), Damien Bonnet (4)

(1) Centre Chirurgical Marie Lannelongue, M3C, Chirurgie des cardiopathies Congénitales, Le Plessis-Robinson, France – (2) Inserm UMR S953, UPMC, Université Paris-6, Paris, France – (3) Institute of Child Health, University College, Cardiac unit, London, Royaume-Uni – (4) AP-HP, CHU Necker-Enfants Malades, Paris, France

Background: Classification of the overall spectrum of congenital heart defects (CHD) has always been challenging, because of the diversity of the cardiac phenotypes and the often complex associations. The purpose of the study was to establish a comprehensive and easy-to-use classification of CHD for clinical and epidemiological studies based on the long list of the International Paediatric and Congenital Cardiac Code (IPCCC).

Methods: We coded each individual malformation using six-digit codes of the long list of IPCCC. We then regrouped all lesions into 10 categories and 22 subcategories according to a multi-dimensional approach encompassing anatomic, diagnostic and therapeutic criteria. This anatomic and clinical classification of congenital heart disease (ACC-CHD) was then applied to data acquired from a population-based study of CHD in France, including 2867 cases (82% live births, 1.8% stillbirths and 16.2% pregnancy terminations).

Results: The majority of cases (79.7%) could be identified with a single IPCCC code. The category “Isomerism and visceral heterotaxy” was the only one that typically required more than one code for identification of cases. The two largest categories were “ventricular septal defects” (52%) and “anomalies of the outflow tract and arterial valves” (20% of cases).

Conclusion: Our proposed classification is not new, but rather a regrouping of the known spectrum of CHD into a manageable number of categories based on anatomic and clinical criteria. The classification is designed to use the code numbers of the long list of IPCCC but can accommodate ICD-10 codes. Its exhaustiveness, simplicity, and anatomic basis make it useful for clinical and epidemiological studies, including those aimed at assessment of risk factors and outcomes. The proposed classification can also provide a structure for various clinical and epidemiologic databases.

Parental electrocardiographic screening identifies a high degree of inheritance for congenital and childhood non-immune isolated atrioventricular defects

Alban-Elouen Baruteau [Orateur] (1), Babak Khoshsood (2), Robert H. Anderson (3), Nathalie Lelong (2), Anne-Claire Thieulin (2), François Goffinet (2), Damien Bonnet (4)

(1) Centre Chirurgical Marie Lannelongue, M3C, Chirurgie des cardiopathies Congénitales, Le Plessis-Robinson, France – (2) Inserm UMR S953, UPMC, Université Paris-6, Paris, France – (3) Institute of Child Health, University College, Cardiac unit, London, Royaume-Uni – (4) AP-HP, CHU Necker-Enfants Malades, Paris, France

Background: Congenital heart disease (CHD) is the most common birth defect, occurring in 0.8% of live births and is responsible for 15% of infant deaths. Atrial septal defect (ASD) is the most common type of CHD, found in 5% of live births. The aim of the study was to establish a comprehensive and easy-to-use classification of CHD for clinical and epidemiological studies based on the long list of the International Paediatric and Congenital Cardiac Code (IPCCC).

Methods: We coded each individual malformation using six-digit codes of the long list of IPCCC. We then regrouped all lesions into 10 categories and 22 subcategories according to a multi-dimensional approach encompassing anatomic, diagnostic and therapeutic criteria. This anatomic and clinical classification of congenital heart disease (ACC-CHD) was then applied to data acquired from a population-based study of CHD in France, including 2867 cases (82% live births, 1.8% stillbirths and 16.2% pregnancy terminations).

Results: The majority of cases (79.7%) could be identified with a single IPCCC code. The category “Isomerism and visceral heterotaxy” was the only one that typically required more than one code for identification of cases. The two largest categories were “ventricular septal defects” (52%) and “anomalies of the outflow tract and arterial valves” (20% of cases).

Conclusion: Our proposed classification is not new, but rather a regrouping of the known spectrum of CHD into a manageable number of categories based on anatomic and clinical criteria. The classification is designed to use the code numbers of the long list of IPCCC but can accommodate ICD-10 codes. Its exhaustiveness, simplicity, and anatomic basis make it useful for clinical and epidemiological studies, including those aimed at assessment of risk factors and outcomes. The proposed classification can also provide a structure for various clinical and epidemiologic databases.

Parental electrocardiographic screening identifies a high degree of inheritance for congenital and childhood non-immune isolated atrioventricular defects

Alban-Elouen Baruteau [Orateur] (1), Babak Khoshsood (2), Robert H. Anderson (3), Nathalie Lelong (2), Anne-Claire Thieulin (2), François Goffinet (2), Damien Bonnet (4)

(1) Centre Chirurgical Marie Lannelongue, M3C, Chirurgie des cardiopathies Congénitales, Le Plessis-Robinson, France – (2) Inserm UMR S953, UPMC, Université Paris-6, Paris, France – (3) Institute of Child Health, University College, Cardiac unit, London, Royaume-Uni – (4) AP-HP, CHU Necker-Enfants Malades, Paris, France

Conclusion: CVD is at least as common in this Djiboutian community as in other African cohorts of children. The absence of surgery was a major mortality risk factor. Dilated cardiomyopathy was frequent in this study. Much work remains to be done to discover the size and nature of genetic and environmental contributions to these various forms of pediatric heart diseases in the Horn of Africa.

Assessment of systo-diastolic ventricular function using tissue Doppler imaging after successful repair of aortic coarctation

Sana Ouali [Orateur] (1), Sami Hammass (1), Helmi Ben Salem (1), Slim Kacem (1), Elyess Neffeti (2), Rim Griba (1), Fahmi Remedi (2), Essia Boughzela (2)

(1) Hopital Sahloul, Cardiologie, Sousse, Tunisie – (2) Hôpital Sahloul, Boughzela (2)

Introduction: The etiology of congenital or childhood non-immune, isolated AV block remains unknown. We hypothesized that this conduction abnormality in the young may be a heritable disease.

Method: A multicenter retrospective study (13 French referral centers, from 1980 to 2009) allowed inclusion of 141 children with AV block diagnosed in utero, at birth or before 15 years of age, without structural heart abnormalities and without maternal antibodies. Parents and matched controls were investigated for family history and for ECG screening.

Results: In parents, family history of sudden death or of progressive cardiac conduction defect was found in 1.4% and 11.1% respectively. Screening ECGs from 130 parents (mean age 42.0 ± 6.8 years, 57 couples) were compared to 130 matched healthy controls. All parents were asymptomatic and in sinus rhythm, except one with unknown complete AV block. Conduction abnormalities were more frequent in parents than in controls, respectively found in 50.8% versus 4.6% (p<0.001). Long PR interval was found in 18.5% parents but never in controls (p<0.001). Complete or incomplete right bundle branch block was observed in 39.2% parents and 1.5% controls (p<0.001). Complete or incomplete left bundle branch block was found in 15.4% parents and 3.1% controls (p<0.001). Heritability estimate for isolated conduction disturbances was very high, calculated at 91% (standard error=0.119, p≤2.10^-10).

Conclusion: ECG screening in asymptomatic parents from children affected by idiopathic AV block revealed a high prevalence of conduction abnormalities with prolongation of intra-atrial, AV and/or intra-ventricular conduction delay. Heritability estimate confirmed a high contribution of genetic factors. These results support the hypothesis of an inheritable trait in congenital and childhood non-immune, isolated AV blocks.

Comparison of PR interval and QRS complex duration

Assessment of systo-diastolic ventricular function using tissue Doppler imaging after successful repair of aortic coarctation

Sana Ouali [Orateur] (1), Sami Hammass (1), Helmi Ben Salem (1), Slim Kacem (1), Elyess Neffeti (2), Rim Griba (1), Fahmi Remedi (2), Essia Boughzela (2)

(1) Hopital Sahloul, Cardiologie, Sousse, Tunisie – (2) Hôpital Sahloul, Boughzela (2)

Introduction: The etiology of congenital or childhood non-immune, isolated AV block remains unknown. We hypothesized that this conduction abnormality in the young may be a heritable disease.

Method: A multicenter retrospective study (13 French referral centers, from 1980 to 2009) allowed inclusion of 141 children with AV block diagnosed in utero, at birth or before 15 years of age, without structural heart abnormalities and without maternal antibodies. Parents and matched controls were investigated for family history and for ECG screening.

Results: In parents, family history of sudden death or of progressive cardiac conduction defect was found in 1.4% and 11.1% respectively. Screening ECGs from 130 parents (mean age 42.0 ± 6.8 years, 57 couples) were compared to 130 matched healthy controls. All parents were asymptomatic and in sinus rhythm, except one with unknown complete AV block. Conduction abnormalities were more frequent in parents than in controls, respectively found in 50.8% versus 4.6% (p<0.001). Long PR interval was found in 18.5% parents but never in controls (p<0.001). Complete or incomplete right bundle branch block was observed in 39.2% parents and 1.5% controls (p<0.001). Complete or incomplete left bundle branch block was found in 15.4% parents and 3.1% controls (p<0.001). Heritability estimate for isolated conduction disturbances was very high, calculated at 91% (standard error=0.119, p≤2.10^-10).

Conclusion: ECG screening in asymptomatic parents from children affected by idiopathic AV block revealed a high prevalence of conduction abnormalities with prolongation of intra-atrial, AV and/or intra-ventricular conduction delay. Heritability estimate confirmed a high contribution of genetic factors. These results support the hypothesis of an inheritable trait in congenital and childhood non-immune, isolated AV blocks.
velocities at the tricuspid and mitral sides were lower in AoC patients than in healthy group. The E/Ea ratio was significantly higher in patients than in control (6.2±2.1 vs 3.8±1, p<0.000). The LV (left ventricular) ejection fraction was not statistically different between AoC group and controls.

**Conclusion:** In late follow-up despite a satisfactory results after surgery repair of aortic coarctation, left and right ventricular systolic and diastolic performance reveals tendency of decrease.

### 343

**Cardiac mechanics in severely obese children: a 2D speckle strain imaging study**

Eva Zangl (1), Fabien Labombarda [Orateur] (1), Arnaud Pellissier (1), Dominique Bougle (2), Jean-Christophe Paon (2), Pascale Maragnes (1), Paul Milliez (1), Eric Saloux (1)

1) CHU Côte de Nacre, Cardiologie, Caen, France – 2) CHU Côte de Nacre, Pédiatrie, Caen, France

**Background:** The prevalence of obesity in children is increasing worldwide. We used 2D speckle strain imaging to investigate whether severely overweight children without hypertension, dyslipidemia, diabetes or sleep apnea, show early cardiac abnormalities. We also investigated the relation between these myocardial features and severity of obesity, fat mass percentage, inflammation and insulin resistance index.

**Methods:** 2D echocardiography, tissue Doppler imaging (TDI) and 2D speckle strain imaging were prospectively performed in obese children and compared to age and sex-matched healthy control subjects. Standard echocardiographic indices of global systolic and diastolic function, early peak diastolic mitral velocity (Ea), longitudinal strain (LS), radial strain (RS) and circumferential strain (CS) were investigated. Z-score body mass index (BMI), body composition, high-sensitive C reactive protein (hs-CRP) and indices of insulin resistance (HOMA-IR) were assessed in the obese children.

**Results:** 32 consecutive obese patients (age: 12.8 [8-17] years; z-score BMI: 5.8 [2.05-8.6]; 15 males; HOMA-IR: 2.1 [0.6-5.7]) were compared to 32 nonobese patients. There was no difference between two groups for left ventricular ejection fraction and conventional diastolic mitral Doppler parameters. Obese subjects showed significantly larger left ventricular wall dimensions (End diastolic diameter: 45±5 vs 43±4 mm; p<0.05; left ventricular mass: 116±31 vs 79±18 g; p<0.005) and signs of early diastolic filling abnormalities on TDI (Ea: 18.1 vs 16.9 cm/s; p=0.02). LS and CS were significantly lower in obese group (LS: –18±2% vs –20±2%; p<0.05; CS: –18±3% vs –20±1±2 %; p<0.05) while RS did not differ. LS and CS were correlated with BMI (Respectively: r=-0.5; p<0.05 and r=0.3; p<0.05). There was no correlation between strain parameters and body composition. There was no correlation between strain parameters and hs-CRP. LS was correlated with HOMA-IR (r: 0.45; p<0.05).

**Conclusion:** Obesity in children is associated with significant impairment of longitudinal and circumferential myocardial strain.

### 344

**Molecular patterning of the cardiac outflow tract and coronary arteries of the mouse heart**

Pauline Parisot [Orateur], Magali Théveniau-Ruissy, Robert Kelly

IBDML, Biologie du Développement du Coeur, Marseille, France

Conotruncal malformations are frequent and often associated with coronary artery anomalies. Coordinated development of the second heart field and cardiac neural crest cells is required to orchestrate outflow tract morphogenesis. Defects in one or other cell type results in a spectrum of conotruncal defects observed in human pathology and mouse models. Tbx1, encoding a T-box transcription factor, is the major candidate gene for DiGeorge syndrome and is required for conotruncal development. Tbx1 +/- mouse embryos have a common arterial trunk and proximal coronary artery patterning defects. In the absence of Tbx1 there is a severe reduction in a subpopulation of second heart field cells contributing to subpulmonary myocardium. Sem3C, encoding a neurovascular guidance molecule, is expressed in a Tbx1-dependent domain in subpulmonary myocardium. Sem3C +/- embryos display common arterial trunk with interrupted aortic arch but coronary artery patterning appears normal. Here we present a comparative analysis of the evolution of common trunk in Tbx1 and Sem3C mouse models. These models of truncus display major anatomical differences visible at early stages in the width and the position of myocardial subdomains of the outflow tract and at fetal stages in truncal valve, coronary and great artery patterning. The Tbx1 null phenotype is similar to pulmonary atresia whereas in Sem3C +/- hearts a hypoplastic aorta emerges from the common trunk leading to an interrupted aortic arch. We also investigated potential genetic interaction between Tbx1 and Sem3C, and identified a cryptic early role of Sem3C in pharyngeal arch artery formation revealed in Tbx1+/- embryos suggesting a potential modifier role of Sem3C in DiGeorge syndrome. In addition, we will present data from a microarray analysis of the migestation mouse outflow tract that has identified additional genes expressed in subpulmonary myocardium, potentially contributing to conotruncal and coronary artery development.

### 345

**Safe treatment of infantile hemangiomas with propranolol despite baseline bradycardia**

Bertille Bonniald (1), Stéphanie Perez-Martin (2), Caroline Bonnet [Orateur] (1), Sylvie Falcon-Eicher (3), Frédéric Huet (2), Pierre Vabres (1)

(1) CHU Dijon, Dermatologie, Dijon, France – (2) CHU Dijon, Pédiatrie, Dijon, France – (3) CHU Dijon, Cardiopédiatrie, Dijon, France

**Background:** The safety profile of propranolol in infantile hemangima (IH) is generally good despite a risk of severe bradycardia. In infants, sinus bradycardia can be a sign of increased vagal tonus, involved in the etiology of the sudden infant death syndrome (SIDS), which occurs in the same age group as IH. In addition, infants with IH may combine several other risk factors for syncope or sudden death. Hence, we aimed to determine the frequency of sinus bradycardia in infants before propranolol initiation and cardiac outcome during treatment in children with baseline bradycardia.

**Methods:** Retrospective observational study of infants treated with propranolol for IH from June 2008 to September 2010 at our institution. Prior to propranolol initiation, a detailed baseline cardiological assessment was systematically performed including cardiac ultrasonography and 24-hour electrocardiographic heart rate monitoring. Further at-home long term monitoring was performed in the infants who had baseline episodes of bradycardia.

**Results:** Significant episodes of sinus bradycardia were found in 3 patients (12.5%), on baseline monitoring prior to propranolol initiation. Cardiorespiratory monitoring at home was thus implemented in these infants and maintained throughout treatment (duration 4 to 8 months). Tolerance was excellent in all three: no further episodes of sinus bradycardia or other adverse events occurred.

**Discussion:** Although asymptomatic, baseline sinus bradycardia may not be uncommon in infants with hemangiomas. It does not seem to preclude the use of propranolol, as no severe sinus bradycardia was noted on propranolol in our series.