

Nat Genet. 2007 Feb;39(2):159-61.

Fanconi anemia is associated with a defect in the BRCA2 partner PALB2.

Xia B, Dorsman JC, Ameziane N, de Vries Y, Roommans MA, Sheng Q, Pals G, Errami A, Gluckman E, Llera J, Wang W, Livingston DM, Joenje H, de Winter JP.

The Fanconi anemia and BRCA networks are considered interconnected, as BRCA2 gene defects have been discovered in individuals with Fanconi anemia subtype D1. Here we show that a defect in the BRCA2-interacting protein PALB2 is associated with Fanconi anemia in an individual with a new subtype. PALB2-deficient cells showed hypersensitivity to cross-linking agents and lacked chromatin-bound BRCA2; these defects were corrected upon ectopic expression of PALB2 or by spontaneous reversion.

Rheumatology (Oxford). 2007 Feb;46(2):314-20.

Health-related quality of life of patients with juvenile idiopathic arthritis coming from 3 different geographic areas. The PRINTO multinational quality of life cohort study.

Gutiérrez-Suárez R, Pistorio A, Cespedes Cruz A, Norambuena X, Flato B, Rumba I, Harjacek M, Nielsen S, Susic G, Mihaylova D, Huemer C, Melo-Gomes J, Andersson-Gare B, Balogh Z, De Cunto C, Vesely R, Pagava K, Romicka AM, Burgos-Vargas R, Martini A, Ruperto N; Pediatric Rheumatology International Trials Organisation (PRINTO).

OBJECTIVES: To compare health-related quality of life (HRQL) and to identify clinical determinants for poor HRQL of patients with juvenile idiopathic arthritis (JIA) coming from three geographic areas.

METHODS: The HRQL was assessed through the Child Health Questionnaire (CHQ). A total of 30 countries were included grouped in three geographic areas: 16 countries in Western Europe; 10 in Eastern Europe; and four in Latin America. Potential determinants of poor HRQL included demographic data, physician's and parent's global assessments, measures of joint inflammation, disability as measured by Childhood Health Assessment Questionnaire (CHAQ) and erythrocyte sedimentation rate. Poor HRQL was defined as a CHQ physical summary score (PhS) or psychosocial summary score (PsS) < 2 S.D. from that of healthy children.

RESULTS: A total of 3167 patients with JIA, younger than 18 yrs, were included in this study. The most affected health concepts (< 2 S.D. from healthy children) that differentiate the three geographic areas include physical functioning, bodily pain/discomfort, global health, general health perception, change in health with respect to the previous year, self-esteem and family cohesion. Determinants for poor HRQL were similar across geographic areas with physical well-being mostly affected by the level of disability while the psychosocial well-being by the intensity of pain.

CONCLUSION: We found that patients with JIA have a significant impairment of their HRQL compared with healthy

peers, particularly in the physical domain.

Disability and pain are the most important determinants of physical and psychosocial well-being irrespective of the geographic area of origin.

Medicina (B Aires). 2007;67(3):253-61.

Congenital adrenal hyperplasia clinical characteristics and genotype in newborn, childhood and adolescence.

Pasqualini T, Alonso G, Tomasini R, Galich AM, Buzzalino N, Fernandez C, Minutolo C, Alba L, Dain L.

Congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency is a disorder which can adopt three clinical expressions: two classical forms

-salt-wasting (SW), with residual enzymatic activity (EA) < or = 1% and simple virilizing (SV), with EA 1-2%- and a mild late onset or nonclassical (NC) form, with EA 10-60%. Our objective is to describe clinical characteristics, growth, and bone mass in a group of patients affected by 21-hydroxylase deficiency.

Besides, molecular genetics studies were performed in patients, and also when available in their parents and siblings. Nine patients with neonatal diagnosis and 8 with pre or postpubertal diagnosis were studied. Analyses of 10-point mutations in the CYP21A2 gene were performed. We found that all the patients with the classical expression, except one with a de novo mutation R356W in one allele, were fully genotyped with predictive < 2% EA mutations. Signs of hyperandrogenism were present in 5/6 NC patients; one was diagnosed by searching for mutations in asymptomatic siblings. All the NC patients were compound heterozygotes carrying V281L mutation in one allele and a predictive low EA in the other, except for one not yet determined. In patients with neonatal diagnosis, mean height was low at one year of age, though it showed a significant increase before the onset of puberty. We conclude that neonatal diagnosis of classical CAH allows an adequate follow up enhancing growth. Molecular analyses of all members of an affected family may disclose asymptomatic patients. The presence of de novo mutations, as well as, the presence of mutations with low predicted EA in NC patients reinforces the importance of genotyping for appropriate genetic counseling. In fully genotyped NC patients, the lowest value of ACTH-stimulated 17OHP was 14 ng/ml. Lower cut-off values might overestimate the diagnosis of the NC form.

Arq Bras Endocrinol Metabol. 2007 Apr;51(3):450-6.

[Phenotype variability in Noonan syndrome patients with and without PTPN11 mutation]

Ferreira LV, Souza SA, Montenegro LR, Arnhold IJ, Pasqualini T, Heinrich JJ, Keselman AC, Mendonça BB, Jorge AA.

INTRODUCTION: Around 50% of Noonan syndrome (NS) patients present heterozygous mutations in the PTPN11 gene. AIM: To evaluate the frequency of mutations in the PTPN11 in patients with NS, and perform phenotype-genotype correlation. PATIENTS: 33 NS patients (23 males).

METHODS: DNA was extracted from peripheral blood leukocytes, and all 15 PTPN11 exons were directly sequenced.

RESULTS: Nine different missense mutations, including the novel P491H, were found in 16 of 33 NS patients. The most frequently observed features in NS patients were posteriorly rotated ears with thick helix (85%), short stature (79%), webbed neck (77%) and cryptorchidism (60%) in boys. The mean height SDS was -2.7 +/- 1.2 and BMI SDS was -1 +/- 1.4. Patients with PTPN11 mutations presented a higher incidence of pulmonary stenosis than patients without mutations (38% vs. 6%, $p < 0.05$). Patients with and without mutations did not present differences regarding height SDS, BMI SDS, frequency of thorax deformity, facial characteristics, cryptorchidism, mental retardation, learning disabilities, GH peak at stimulation test and IGF-1 or IGFBP-3 SDS.

CONCLUSION: We identified missense mutations in 48.5% of the NS patients. There was a positive correlation between the presence of PTPN11 mutations and pulmonary stenosis frequency in NS patients.

Horm Res. 2007;68(5):261-4.

True hermaphroditism in a phenotypic male without ambiguous genitalia: an unusual presentation at puberty.

Alonso G, Pasqualini T, Busaniche J, Ruiz E, Chemes H.

True hermaphroditism usually appears with ambiguous genitalia requiring extensive evaluation during the neonatal period. There have been occasional cases with better differentiation of external genitalia, leading to delays in diagnosis. We report the case of an adolescent boy with true hermaphroditism who presented with normal external genitalia and no sexual ambiguity. He was referred due to progressive gynecomastia and arrest of puberty. He presented at the age of 16 years for gynecomastia of rapid progression with normal penile development and both gonads in scrotum and normal testosterone and increased gonadotropin levels.

Gonadal ultrasound scan was compatible with testicular and ovarian tissues in scrotum, and the karyotype showed two cellular lines (46,XX/46,XY). Gonadal histology revealed bilateral ovotestes. A genotype polymerase chain reaction mediated analysis using seven microsatellite markers did not confirm chimerism. Clinical findings and mechanism of generation are discussed.

Pediatr Nephrol. 2007 May;22(5):734-41.

Effects of deflazacort vs. methylprednisone: a randomized study in kidney transplant patients.

Ferraris JR, Pasqualini T, Alonso G, Legal S, Sorroche P, Galich AM, Jasper H; The Deflazacort Study Group.

Metabolic effects of deflazacort vs. methylprednisone were studied in prepubertal patients after kidney transplantation. Thirty-one patients participated: 15 received deflazacort and 16 remained on methylprednisone. The study started at a mean of 2.1 years after transplantation, when patients were randomized to either continue with methylprednisone or switch to deflazacort. Height velocity increased more in the deflazacort than in the methylprednisone group only during the first 2 years: 5.4 +/- 0.5 vs. 3.5 +/- 0.3 cm/year, and 4.2 +/- 0.8 vs. 2.2 +/- 0.4 cm/year $p = 0.007$, [by two-way analysis of variance (ANOVA)]. After 2 and 3 years, the number of patients who were overweight increased in the methylprednisone group and decreased in the deflazacort

group; $p < 0.01$. Lean body mass increased more in the deflazacort than in the methylprednisone group ($p = 0.003$). Fat body mass increased only in the methylprednisone group ($p < 0.01$). Total cholesterol and low-density-lipoprotein (LDL) cholesterol increased in the methylprednisone group ($p < 0.05$ and $p < 0.01$, respectively). Total and LDL cholesterol were reduced ($p < 0.01$ and $p < 0.001$, respectively), whereas high-density-lipoprotein (HDL) cholesterol increased ($p < 0.001$) during deflazacort therapy. Lumbar spine bone mineral density (BMD) decreased in both groups, but total skeleton BMD decreased only in the methylprednisone group ($p < 0.001$). Finally, normal glucose/insulin ratio, defined as > 7 , was associated ($p < 0.05$) with the deflazacort group. Our data suggest that deflazacort therapy might improve linear growth and lean body mass and prevent excessive bone loss and fat accumulation. It also leads to an improvement in lipoprotein profile without reduction in insulin sensitivity.

J Pediatr. 2007 Apr;150(4):418-21.

Pre-ductal and post-ductal O2 saturation in healthy term neonates after birth.

Mariani G, Dik PB, Ezquer A, Aguirre A, Esteban ML, Perez C, Fernandez Jonusas S, Fustiñana C.

OBJECTIVE: To determine the pre- and post-ductal oxygen saturation (SpO₂) levels during the first minutes after birth in healthy term infants.

STUDY DESIGN: In a prospective cohort study, sensors were placed on the right hand and on 1 foot of the neonate. Pre- and post-ductal SpO₂ levels were recorded during the first 15 minutes after birth. Exclusion criteria were gestational age < 37 weeks, presence of risk factors for asphyxia, emergency cesarean delivery (C/D), congenital anomalies, and multiple pregnancies. Infants who were treated with O₂ or positive pressure ventilation were also excluded from the study.

RESULTS: The mean (SD) gestational age of the 110 infants was 39 weeks (1.1), and the mean birth weight was 3340 grams (359). At 5 minutes, the mean pre-ductal SpO₂ level was 89% (7), and the mean post-ductal SpO₂ level was 81% (10). Pre- and post-ductal SpO₂ levels were significantly different during the first 15 minutes after birth. The SpO₂ level was lower in babies delivered by C/D in comparison to babies born by vaginal delivery.

CONCLUSIONS: In healthy newly born infants, oxygen saturation rises slowly and does not usually reach 90% in the first 5 minutes of life. A gradient between pre- and post-ductal SpO₂ levels remains significant for the first 15 minutes of life.

Pediatr Crit Care Med. 2007 Sep;8(5):489-91.

Internal mammary artery injury after central venous catheterization.

Fulmesekian PG, Pérez A, Mincos PG, Lobos P, Moldes J, García Mónaco R.

OBJECTIVE: We describe an infrequent but potentially lethal complication: an iatrogenic injury of the internal mammary artery after central venous catheterization.

DESIGN: Report of cases. **SETTING:** Pediatric intensive care unit. **PATIENTS:** The first patient we report on is a 3-yr-old girl who was severely neurologically damaged and was admitted to the pediatric intensive care unit for aspiration pneumonia and septic shock. Immediately after vein cannulation on the left internal jugular vein, the patient suffered hypotension and cardiac arrest, secondary to an adequately drained massive hemothorax. Restoration of

spontaneous circulation was initially achieved, and the patient was transferred to the angiographic suite. Selective angiography during cardiopulmonary resuscitation for a second cardiac arrest revealed a laceration of the internal mammary artery. Resuscitation was not successful, and the patient died. The second case reported is a 7-yr-old girl admitted for bone marrow transplantation. She was electively taken to the angiographic suite for central venous insertion. An infraclavicular approach of the right subclavian vein was attempted, but radioscopy showed the guidewire inside the pleural space. Soon thereafter, the patient became hypotensive and was in shock. Radioscopy showed a large pleural effusion and a massive hemothorax was drained. Selective angiography demonstrated an injured internal mammary artery was embolized. Hemodynamics improved, and the patient was transferred to the pediatric intensive care unit, where she was extubated 12 hrs later.

INTERVENTIONS: None.

CONCLUSIONS: Central venous catheter placement in the intrathoracic vein may cause potentially lethal complications in the form of an injury to the internal mammary artery. Hypotension during or immediately after the procedure should be a warning of a serious adverse event, such as massive hemothorax, that may compromise life. Adequate drainage of the pleural cavity may not completely relieve vascular compression if some of the bleeding from an injured internal mammary artery is extrapleural. Early diagnosis and treatment by selective embolization of the injured vessel in interventional radiology is the first therapeutic choice and may be life saving.

Pediatr Crit Care Med. 2007 Jan;8(1):54-7.

Validation of pediatric index of mortality 2 (PIM2) in a single pediatric intensive care unit of Argentina.

Eulmesekian PG, Pérez A, Mincos PG, Ferrero H.

OBJECTIVE: Pediatric Index of Mortality 2 (PIM2) is an up-to-date mortality prediction model in the public domain that has not yet been widely validated. We aimed to evaluate this score in the population of patients admitted to our pediatric intensive care unit.

DESIGN: Prospective cohort study. **SETTING:** Multidisciplinary pediatric intensive care unit in a general university hospital in Buenos Aires, Argentina. **PATIENTS:** All consecutive patients admitted between January 1, 2004, and December 31, 2005.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: There were 1,574 patients included in the study. We observed 41 (2.6%) deaths, and PIM2 estimated 48.1 (3.06) deaths. Discrimination assessed by the area under the receiver operating characteristic curve was 0.9 (95% confidence interval, 0.89-0.92). Calibration across five conventional mortality risk intervals assessed by the Hosmer-Lemeshow goodness-of-fit test showed $\chi^2 = 12.2$ ($p = .0348$). The standardized mortality ratio for the whole population was 0.85 (95% confidence interval, 0.6-1.1). **CONCLUSIONS:** PIM2 showed an adequate discrimination between death and survival and a poor calibration assessed by the Hosmer-Lemeshow goodness-of-fit test. The standardized mortality ratio and clinical analysis of the Hosmer-Lemeshow table make us consider that PIM2 reasonably predicted the outcome of our patients.