Trabajos enviados a Congresos y/o publicados en revistas Internacionales por los profesionales del HCUCh durante el año 2001*

** En el número 1 del año 2002 (volumen 13), se publicó, como cada año, los abstracts recibidos en la redacción. Por errores de variada índole, los que aparecen a continuación no fueron publicados en dicha ocasión y los publicamos ahora por su interés para la comunidad académica con nuestras disculpas a sus autores.*

Rev Med Chil. 2001 Mar;129(3):277-84. European Journal of Human Genetics 2001; S1: P1014

Impact of wheat flour fortification with folic acid on the prevention of neural tube defects (NTD) in Chile: preliminary results.

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Starting in January 2000, the Chilean Ministry of Health legislated to add folic acid (FA) to wheat flour (2.2 mg/kg). Chilean women of low socioeconomic status (70% of the population) consume high amounts of bread (mean: 200g/day) which would provide 330 ug/day of FA. To determine the effectiveness of this fortification we are monitoring folate status of child bearing age women and the rates of NTD in Chile. Folate status was assessed in 750 women of reproductive age from low socioeconomic level in Santiago, before and one year after fortification. Frequencies of NTD will be recorded from 1999-2000 (baseline) to 2002, in around 60.000 births/year occuring in the nine public maternity hospitals of Santiago. Serum and red blood folates values of chilean women before fortification are similar to those of US non supplemented women before grain FA fortifiction (NHANES II). Samples to measure folate levels after fortification in the same group were obtained recently. Results are being processed. The frequency of NTD in Santiago before fortification, including year 1999 up to September 2000, in 103.554 newborns (alive and stillbirths, over 500g of birth weight) was 1,69/1000. Rates were 1,32/1000 and 49,93/1000 in alive newborns and in stillbirths respectively. Rates of each defect were anencephaly 0,56/1000; encephalocele 0,25/1000 and spins bifida 0,88/1000. All defects were more frequent in females (61,1% vs 37,7%, p=0.001). According to folic acid supply from bread, we expect that babies born under the effect of the intervention at conception will start by January 2001, so we will bw able to show the results from the first trimester of 2001 at the Congress.

Supported by March of Dimes, Center for Disease Control and Prevention, Chilean Ministry of Health, PAHO / WHO.

European Journal of Human Genetics 2001; S1: P0250

Translocation and Spontaneous Abortions

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Chromosomal anomalies usually invoked as one important etiology that should be considered, when a couple has spontaneous abortions. In this work we present the results of 481 cytogenetic studies corresponding to 382 (79,4%) positive cultures, and 162 (42%) had chromosomal alteration. The most frequent structural alterations were desbalanced translocations (6,2%). We studied five pairs (50%) of parents of this group, and we fond always a balanced translocations in one of them. We believe that the high ratio of translocations in the parents may be reflecting more frequent chromosomal rearrangements in the descendants of couples with balanced translocations as has been recently suggested in the preimplantational studies.

European Journal of Human Genetics 2001; S1: P0170

Cytogenetic alterations in hematological malignancies

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Among 518 cytogenetic studies dome in hematological malignancies, we had 52 failures (10%). Normal results represented 290 cases (56%), expected when controlling remissions or uncertain diagnosis. Different aberrations were found in 176 cases (34%). The total number of studied patients is 386, many of them have repeted controls, the pediatric population is 78 (20.2%). The most frequent reference diagnosis were acute myeloid leukemia (15.»%), chronic myeloid leukemia (12,3%), acute lymphoid leukemia (11,6%), myeloidysplasia (11,2%), and multiple myeloma (7,6%). The most common cytogenetic finding was t(9;22)(q34;q11) in 76 studies (43%), either isolated or with additional aberrations. We also performed FISH studies in 57 patients ; in 25 cases with X and Y probes for control of grafting of bone marrow transplantation with a non-sex matched relative; in 15 cases in search of t(9;22) (q34;q11) with 1 positive result. We intend to clarify some complex cases with many marker chromosomes with multiple FISH or comparative genomic hybridisation

33 Reunión Anual ECLAMC: Estudio colaborativo latinoamericano de malformaciones congénitas, 4 – 9 noviembre 2001, Angra dos Reis, Brasil

Clinical case

Pardo A.

This 2 year- old boy, was the product of the first pregnancy of a 28 year old mother and ended with a vaginal delivery at 38 weeks gestation. There were symptoms of spontaneous abortion in the second and third months, controled without medication. Birth weight was 3500g, length was 52 cm and head circumference was 32 cm. Apgar score is unknown. The pediatrician noted cranial asimmetry and skull radiography demonstrated a craneosynostosis of the coronal suture. At age 7 months, he had neurosurgery, because of intracranial hypertension. The neuropediatric controls report mild retarded development, hypotonia. Now, he receives physical rehabilitation. At 2 years- 2 months, his weight was: 15,2 K (< 1DS), length was: 99 cm (> 3 DS) and head circumference

was: 50 cm (P 50). He has plagiocephaly, left palpebral ptosis, up-slanting palpebral fissures, strabism, hypertelorism, deep-flattened nasal bridge, long philtrum, thin lips, and flat face. He has also right cryptorchidia, joint hypermobility, and the 2nd left toe bent over the 1st left toe. He walkes with short and dull steps.

His caryotype is 46, XY. Metabolic screening and orine mucopolisaccarides were normal. Feet and hand X-rays, as well as hormonal studies for his tall stature are in course. His sister has epilepsy, an aunt and great uncle have miopia and right palpebral ptosis. ID: Jackson-Weiss syndrome.

33 Reunión Anual ECLAMC: Estudio colaborativo latinoamericano de malformaciones congénitas, 4 – 9 noviembre 2001, Angra dos Reis, Brasil.

Clinical Case

Aravena T.

JARO, a 2-month old girl, was born after a 36-week long pregnancy complicated with symptoms of spontaneous abortion in the seventh week, controlled without medication. She had prenatal ultrasonographic diagnosis of cleft lip at 20 weeks gestation. She was the first child of non consanguineous parents, the mother was 31 years old and father was 43 years old. Together they had a previous molar pregnancy and both had healthy children with other couples. The father takes fluoxetine and antihypertensive drugs. Birth weight 2755g (< 1DS), birth length 47,5cm (< 1DS), apgar score 8 –9. When examined at 12 days, she had hypotonia, turricephaly, upslanting palpebral fissures, cleft left lip and palate, low set ears, areolar hypoplasia, sistolic murmur G II/ VI, anterior anus, pilonidal foseta, clinodactyly of fifth digits, ungueal hypoplasia. At 6 months her weight was 5760g (P5), length was 66cm (P50) and head circumference was 41,2 cm (P50), she had plagiocephaly, ocular hypertelorism, strabism, deep- flattened nasal brigde, pectum carinatum, muscular hypoplasia and persistent hypotonia. She has retarded psicomotor development. Echocardiography: ventricular septal defect and auricular septal defect, actually with digitalics and furosemide, and cardiologic controls. Normal encephalic ultrasonography. Magnetic nuclear resonance: mild temporal and frontal cortical «expansion» (¿?), white substance with mild retarded maduration. Normal renal ultrasonography: normal. Hip radiography: luxation of right hip, in orthopedic treatment. G- banded caryotype: 46, XX, dup(7)(p15) Multiple banding shows this same cytogenetic finding in coloured bands. Strabism with ophthalmologic treatment. Hypotonia in physical rehabilitation. Low weight in nutricional recuperation. Maxilofacial orthopedic treatment with oro-nasal plate.

33 Reunión Anual ECLAMC : Estudio colaborativo latinoamericano de malformaciones congénitas, 4-9 noviembre 2001, Angra dos Reis, Brasil.

Unknown craneosinostosis syndrome with severe malformations of extremities

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First daughter of a young and healthy couple, aged 18 and 21 respectively. Both are university students, she ocasionally used neopren (adhesive with organic solvents) for her archi-

tecture works. No history of use or abuse of potential teratogens. Pregnancy was uncovered until the 6th month; the mother received poor medical care. An elective cesarean section was performed at 36 weeks gestation because of severe oligoamnios, intrauterine growth retardation and suspicion of multiple malformations. Birth weight 2.025g Length was not measured. Head circumference 29,5cm Apgar 8 – 9 Physical examination : turricephaly with wide fontanels, an osseus structure is felt in the medial frontal zone. Shallow orbital ridges with ocular proptosis. Mongoloid slant inclination of palpebral fissures. Beaked nose. Soft palatal cleft. Narrow elfin-like ears. Micrognatia. Prominent and high occiput. Abundant redundant skin on the neck. No cardiac murmurs. Prominent and sharp xifoid appendix. Liver and spleen are palpable on abdomen. Normal female genitalia. Normal extremities in proximal segments, shortened and curved medial segments with skin dimples in median region, deviated hands and feet with oligodactyly in superiors and partial syndactyly. G-banded cariotype: 46,XX. Normal echocardiogram and abdominal ultrasonography. Brain scan: normal cortical mantle. Stenosis of posterior fossa and small foramen magnum. Normal corpus callosum. Normal blood count and platelet count. Radiological study: bilateral radius agenesis, 90° angulation of both hands, right hand: absence of middle finger and presence of three metacarpal bones, one as an additional bud, syndactyly. Left hand: presence of thumb and three fingers, agenesis of little finger? Absence of both fibulae, varus deviation of metatarsal bones. Cranium: increased anteroposterior diameter, multiple radiolucent images. Spine bones: tall vertebral bodies.

XVII Reunión de la Asociación Latinoamericana de Reproducción Humana Curitiba, Brasil. Mayo 2001

El factor de crecimiento nervioso (NGF) induce la expresión de los receptores de FSH funcionales en ovarios inmaduros

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Nuestro objetivo fue saber si NGF además de ser importante en la proliferación celular en el ovario inmaduro, era capaz de inducir la expresión de los receptores de FSH (FSH-R) en ovarios inmaduros y si éstos eran fisiológicamente activos.

Para responder a nuestro objetivo se realizaron dos tipos de experimentos: a) ovarios de ratas de dos días de vida cultivados por 8 h con NGF (100ng/ml), se usó Forskolina (1uM y 20 uM) como control positivo. Al término del cultivo los ovarios fueron guardados a –85°C hasta la extracción de RNA y posterior RT-PCR cuantitativo para determinar la concentración de FSH-R y en el medio de cultivo se determinó la concentración de AMPc. b) al igual que en a, sólo que se usó además como control positivo VIP (2uM) y el cultivo continuó por 32 horas con cambio de medio a las 8 para agregar FSH (500 ng/ml NIH-ovine FSH-S-16) por 24 horas con cambio de medio nuevamente a las 12 horas para determinar la concentración de AMPc. Todos los tratamientos se realizaron en presencia de

IBMX 0.5 mM. Al término de las 32 h de cultivo, los ovarios fueron fijados en solución Kahle, para realizar el análisis morfométrico.

Los resultados demuestran un aumento significativo del RNAm para el receptor de FSH por efecto de NGF ($p < 0.01$), así como también un aumento aditivo del RNAm para FSH-R cuando se usa NGF junto con Forskolina 1uM ($p < 0.01$), sin embargo este efecto no sería mediado por un aumento de AMPc. Tanto NGF como VIP inducen la aparición de receptores de FSH fincionales, ya que los ovarios al ser tratados posteriormente con FSH tienen la capacidad de estimular la formación de AMPc ($p < 0.025$). Además, los ovarios que estuvieron en presencia de NGF y posteriormente con FSH tienen un mayor número de folículos de tres o mas capas de granulosa ($p < 0.01$).

Se concluye que una de las funciones de NGF en el ovario en desarrollo es facilitar el proceso de diferenciación celular por el cual los folículos se hacen dependientes a gonadotrofinas a través del aumento de la síntesis de receptores a FSH.

(Financiado por grant del NIH, HD 24870, RR-00163 y NICHD- U54-18185).

XXI RADLA, Foz de Iguazú, Mayo 2001

Melanoma maligno en Santiago - Chile 1992-1998*

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* Este trabajo obtuvo un premio en la categoría Dermatología Joven en este Congreso.

El melanoma maligno (MM) constituye el cáncer cutáneo de pronóstico más reservado. Su incidencia muestra una tendencia al ascenso en la población de raza blanca a nivel mundial. En América Latina en general, existen escasos reportes sobre la incidencia real del MM en la población.

Se realizó un estudio retrospectivo analizando los MM registrados en cinco hospitales de Santiago de Chile, que cubren un 70% (equivalente a 1.860.000 habitantes) de la población beneficiaria del Fondo Nacional de Salud entre el 1°de enero de 1992 y el 31 de diciembre de 1998.

Se estudiaron 432 MM, presentándose con mayor frecuencia en mujeres (58.6% versus 41.4% en hombres). El intervalo de edad más frecuente fue en mayores de 65 años, con una edad promedio de 61 años. Según localización, el mayor porcentaje de tumores se presentó en pies (17.8%) seguido de piernas (16.6%) y mejillas (14.5%). El tipo clínico más frecuente fue el nodular (33.1%), seguido del superficial extensivo (20.8%). La mayor parte de los tumores eran invasivos (71%), con un 19% de lesiones in situ. El espesor promedio de los tumores fue de 2932.5 micras.

Según el tiempo estudiado, los tumores de zonas fotoexpuestas presentaron incremento en su incidencia desde 1992 en un 158% y un riesgo relativo de 2.58 veces más posibilidades de presentar un MM en ubicación fofoexpuestd en 1998 que en 1992.

Este estudio epidemiológico es el primero en su género realizado en nuestro país, que cuenta con un número importante de casos analizados. Por otro lado, nos muestra que el MM en Chile presenta una tendencia al ascenso según la muestra estudiada, lo cual debe enfocarnos hacia el estudio de estrategias preventivas eficaces, que nos permitan realizar un diagnóstico precoz de MM en nuestra población.