# 23

CHILEAN SCREENING PROGRAM FOR CONGENITAL HYPOTHYROIDISM. PSYCHOMETRIC AND NEUROLOGICAL EVALUATION OF DETECTED CASES.
Cuello, X., Abodovsky, N., Vivanco, X., Pérez, P., Manríquez, M., Godoy, X. San Juan de Dios Hospital, INTA, University of Chile, Santiago, Chile.
This national program has detected 35 patients in the Metropolitan Region and 6â Region, from March, 1992 until May, 1994. The observed incidence is 1/4316.
Objective: Psychometric and neurological evaluation of the subjects detected. Method: Psychometric evaluation by psychologist, applying Bayley scales and neurological evaluation by pediatric neurologist, at 2-6-10-12-18-24 months of age. Results: Out of 33 children: 24 had initial low T4, 6 had compensated hypothyroidism (HCT) and 3 had delayed hypothyroidism (HCT). Out of 24 patients, 23 began their treatment at an average age of 16 days. Initial T4 was 5.85 µg/dL (range: 1.0-9.9). Psychometry was normal at all ages. One case was treated at 73 days, with T4 0.1 µg/dL and had altered psychometry, which tended to improve later on. Comparing six patients with delayed bone age (BA) and average T4 2.65 µg/dL (range: 0.1-4.8) with 18 patients with normal bone age and average T4 5.85 µg/dL (range: 1.0-9.9) psychometry was normal in both groups, but tended to have higher scores in the cases with normal BA. All HC and HCT psychometric tests were normal, except in one who had a marginal score at 3 months of age. Neurological examination was abnormal in 3 out of 24: one whose treatment was delayed, one preterm child with a pyramidal syndrome at 3 months of age, and 1 with slight psychomotor delay at 3 months of age.
Conclusions: 1.- After 18 months of observation the psychometric tests were normal when treatment was started before the age of 30 days. 2.- Delayed (BA) and low T4 level (< 4.28 µg/dL) may predict retarded psychomotor development. 3.- It is necessary to have longer follow up in order to predict psychomotor development.

# 24

RELATION OF LIPOPROTEIN (a) TO PARENTAL CARDIOVASCULAR DISEASE.
Asenjo,S., Casanueva, V., Calvo, C., Cid. X., Ernst, I., Wilhelm, V., Gleisner, A. Departments of Pediatrics and Biochemistry, University of Concepción, Chile.
Lipoprotein a (Lp(a)) is considered as a risk-indicator for cardiovascular disease (CHD), independent of known factors such as hypercholesterolemia, obesity, diabetes mellitus and hypertension.The aim of this study was to determine whether Lp(a) plasma concentrations in children with parents with CHD below 45 years of age is a useful risk indicator for this disease, and to establish the relationship with ethnic factors. 18 Caucasian children aged 4-15 years with parental CHD (Group A) were studied and compared with 71 Caucasians without parental CHD (group B) and 44 Pehuenche children living in Alto Bío Bío (group C). Lp(a) was measured in serum by enzyme immunoassay using monoclonal antiapo(a) as antibody and polyclonal anti apoB peroxidase to avoid cross reaction with plasminogen. Lp(a) values higher than 30 mg/dl were considered risk indicators for CHD.
In 15 children (83%) of group A, 59 (83%) of group B, and 42 (95%) of group C Lp(a) values were ≤ 30 mg/dl. None in group A, 3 (4.2%) in group B and 2 (4.5%) in group C had Lp(a) levels between 31-50 mg/dl. Three (16.6%) in group A, 9 (12.6%) in group B, and none in group C had Lp(a) levels > 50mg/dl. In group A the relative risk was 1.3 times higher compared with group B and 16.6 times higher compared with group C. When considering Lp(a) values of 31-50 mg/dl there are no relative risk differences between group A and B (RR:0.98) but there is relative risk difference in comparison with group C (RR:3.68).
CONCLUSIONS: Lp(a) levels > 50 mg/dl pose a greater risk for CHD in Caucasian children with parental CHD compared with the general Caucasian population, and a much greater risk than in the Pehuenche population. Lp(a) levels between 31 and 50mg/dl pose a greater risk in Caucasians only when compared to the Pehuenche population. These results support the hypothesis that Lp(a) may be influenced by ethnic factors.

# 25

IMPRINTING EFFECT OF FETAL AND/OR PERINATAL ADRENAL STEROIDS ON SERUM LH IN 21-HYDROXYLASE DEFICIENCY (CAH).
Belgorosky, A., Chain, S.,Rivarola, M.A., Laboratory of Investigation. Garrahan Children's Hospital, Buenos Aires, Argentina.
Serum LH levels are lower and serum FSH levels are higher in girls than in boys during the first trimester of postnatal life. The mechanism for these sex differences is not known. In order to study the influence of high levels of adrenal steroids, mainly androgens and progestins, on serum gonadotropins during this period of life, 9 girls with CAH, mean ± SD age 20.9±15.8 days, were studied before and after 56±41 days of oral hydrocortisone replacement therapy. A control group of 16 girls (C1) and 15 boys (C2), mean ages 41.7±33.6 and 59.3±43.3 days, respectively, were also studied. Serum LH and FSH levels were determined by enzyme immunoassay in the presence of two monoclonal antibodies. Mean serum LH in untreated CAH patients (1.28±1.91 IU/L) was higher than in C1 (0.47±0.38) and lower than in C2 (2.52±1.74), but differences were not statistically significant. Mean serum FSH in untreated CAH patients (2.19±3.25 IU/L) was significantly lower ($p < 0.05$) than in C1 (6.57±5.23), but similar to C2 (2.43±1.67). During therapy, serum LH in CAH patients (3.49±4.82) was significantly higher than in C1 , ($p < 0.02$) and similar to C2; while serum FSH in CAH patients (3.72±1.78) was not different than in C1 or C2. These data suggest that high levels of adrenal steroids, probably androgens, might modulate gonadotropin secretion at the hypothalamic or pituitary level. These steroids might exert a synergistic inhibitory effect with ovarian inhibin on FSH secretion in these girls. The fact that after adrenal steroid suppression, the pattern of serum LH levels in these infant girls with CAH remained similar to that of control boys, suggests that high levels of androgens at a critical period during fetal and/or perinatal life, had an imprinting effect on the control of LH secretion that persists after androgen withdrawal.

# 26

TRUE HERMAPHRODITISM (TH): CLINICAL, CYTOGENETICAL AND HISTOLOGICAL STUDIES AND MANAGEMENT OF 10 BRAZILIAN CASES.
Guerra Jr.,G., Maciel-Guerra,A.T., Marques-de-Faria,A.P., Baptista,M.T.M., Silva,R.B.P., Ceschini,M., Cardinalli,I.A. Interdisciplinary Group for the Study of Sexual Development - GIEDDS - FCM-UNICAMP - Campinas - Sao Paulo -Brasil.
The frequency of TH as cause of ambiguous genitalia (AG), as well as the cytogenetic features and gonadal histology, depend on the population studied. Among 126 cases of AG seen at the GIEDDS during the past 5 years, 10 exhibited TH (7.9%). The mean age was 78 months (range 2 to 239 months). Nine patients were assigned as males, probably due to a high degree of virilization of the external genitalia (phallus with mean length of 3 cm, 6 cases with complete labioscrotal fold fusion, and 8 with at least one palpable gonad). There was no consanguinity, and in 2 instances there were familial cases of AG. The karyotype was 46,XY in 4 cases, 46,XX in ?, 46,XX/46,XY in 2, 45,X,+ mar. in 1, and 45,X/47,XYY in 1. Concerning the internal genitalia, in 9 cases there were Fallopian tubes, uterus in 8, and vas deferens in 4. The histological study of the 20 gonads (gonadectomy in 15) demonstrated 8 testes (T), 6 ovaries, 4 ovotestes (OT). Gonads were not found in 2 (GNF), but there was evidence of previous testicular function (mullerian regression and wolffian development). One 7 year old case (46,XY) exhibited bilateral gonadoblastomas. In 60 % of cases there was bilateral TH and the remainder were unilateral, 2 with OT + T and 2 with OT + GNF. The social sex was changed (male to female) in 4 patients. These results are quite different compared to other regions of the world, such as South Africa, Japan and Europe.

# 27

PAPILLARY THYROID CARCINOMA (Ca) IN CHILDREN AND ADOLESCENTS: DIFFERENCES IN AGGRESIVENESS AND NEW STRATEGY OF FOLLOW UP.
Iorcansky, S., Moguilevsky, J., Zantleifer, D., Gallo, G. Departments of Endocrinology, Nuclear Medicine and Pathology, Garrahan Children's Hospital, Buenos Aires, Argentina.
The new histologic approach to papillary thyroid Ca includes subtypes with poor prognosis (those with solid areas, diffuse infiltration, tall and columnar cell types), and others with good prognosis (encapsulated and predominantly follicular types).
A total group of 15 patients (ages X±SD 11.4±4.5yr, females, 12, males, 3) with a follow up of 1 to 6 years, was re-evaluated. Two had diffuse Ca with massive involvement of the gland, lymph nodes and miliary lung infiltration. Both cases had very high serum levels of calcitonin, X:220 pmol/L (normal value < 29 pmol/L) without areas of medullary carcinoma. Twelve tumors were of the conventional type and one was encapsulated.
Post-operative follow up was performed with thyroglobulin (Tg) measurements every 3 months (normal value for athyreotic patients: < 6 ng/ml) and total body scans every 6 to 12 months. Patients with residual thyroid tissue had Tg values over 14 ng/ml. Patients without tumor showed Tg < 3 ng/ml. A new strategy of follow up was carried out in 7 patients by using Thallium-201 (Tl-201), a radiotracer of low radiation energy, without discontinuing l-thyroxine (T4) treatment. Results were compared with conventional scintigram, performed with 5-10mCi I-131 after 30 days of discontinuing T4. Findings coincided in all patients using either Tl-201 or I-131. In conclusion: Diffuse Ca were more aggressive so total thyroidectomies were performed in them, as well as in conventional types. The encapsulated Ca were treated with subtotal resection. According to the results of Tg values and Tl-201 scintigrams, we propose to restrict I-131 scans to patients with abnormal Tg values and/or residual thyroid tissue on Tl-201 scan. Thus, both the interruption of l-T4 treatment and the I-131 high radiation may be avoided in patients in whom treatment with I-131 is not necessary.

# 28

CABERGOLINE (CAB) TREATMENT FOR HYPERPROLACTINEMIC AMENORRHEAS IN ADOLESCENCE. Fideleff,H.L., Wainstein,L., Chervin,A., Vitale, M., Pagano,S.M., Holland,M. Division of Endocrinology, Alvarez Hospital, Buenos Aires, Argentina.
Dopamine agonists represent the treatment of choice for hyperprolactinemic amenorrheas during adolescence. In order to evaluate a new long-acting drug CAB (1-[6 allylergolin-8-ß-il-carbonyl]-1-[3(diethylamino)propyl]3-ethylurea) we studied 5 hyperprolactinemic adolescents with a chronological age between 16 and 18 years (1 microadenoma, 2 residual hyperprolactinemias following pituitary adenoma surgery and 2 idiopathic hyperprolactinemias). Four of them received bromocriptine (BEC) during 24 weeks. Prolactin (PRL) was measured basally and after 4,8,12,16,20 and 24 weeks of treatment. After a 4 week wash-out period, CAB was administered and PRL was measured basally and at monthly intervals for 48 weeks. The fifth patient only received CAB treatment for 48 weeks. BEC was administered at variable doses of 2.5 mg three or four times per day, and CAB was administered at a single weekly dose of 0.5 to 1mg. Serum PRL was measured by RIA and statistical evaluation was performed with Wilcoxon's test. Results are presented in the table (mean ± SEM).

| PRL(ng/ml) | BASAL | 4 WEEKS | 24 WEEKS | 48 WEEKS |
|---|---|---|---|---|
| BEC | 136.9±53.5 | 49.5±5.5 | 36.2±6.4 | |
| CAB | 180.5±73.4 | 34.6±8.7 | 28.2±7.6* | 38.4±15.6* |
| | $p < 0.5$ | $p < 0.5$ | $p < 0.07$ | |

* CAB 24 weeks vs. CAB 48 weeks $p < 0.7$
All patients resumed menstrual and ovulatory cycles. No tumor relapse was observed in the patients with residual hyperprolactinemias following pituitary surgery, whereas in the patient with microadenoma no tumor was visualized on CT at 48 weeks. Conclusions: 1) At 24 weeks there were no significant differences in the PRL values observed in patients treated with BEC or CAB, 2) The effect achieved with CAB persisted at 48 weeks. 3) CAB was effective in restoring gonadal function, mantaining asymptomatic patients who had undergone pituitary surgery and causing the tumor image to disappear. 4) Due to its long - acting properties, its ease of administration, and its low incidence of side-effects, CAB appears to be a useful treatment for hyperprolactinemia in adolescents.