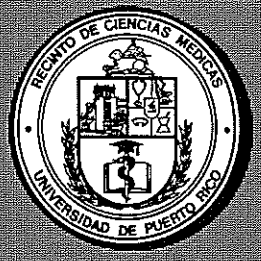

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ABSTRACTS

Apoptosis, Oncology and HIV Infection

A-1 VACCINE EVALUATION STUDIES OF REPLICATION-DEFECTIVE $SIV_{SM}B7$.

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Non-infectious virus-like particles of SIVsmB7 that expresses env and gag gene products but are defective in pol and vpx/vpr were assessed for their ability to induce protective immunity against infection with pathogenic SIVsmE660 in rhesus macaques. Animals were immunized in three groups: group A was primed with cell-associated SIVsmB7 and boosted with cell-free SIVsmB7; group B was primed with cell-free SIVsmB7 and boosted with cell-free SIVsmB7 conjugated to iron oxide microbeads; group C was primed with cell-free SIVsmB7 mixed with Titer Max adjuvant and boosted with cell-free SIVsmB7 mixed with SAF-M adjuvant followed by secondary boosting with cell-free SIVsmB7 conjugated to microbeads. Animals were challenged intravenously with 20 animal infectious doses of SIVsmE660 grown in rhesus peripheral blood mononuclear cells 3 weeks after final boosting. All animals became infected as evidenced by quantitative virus cultivation. Sera from immunized animals contained low-titer antibodies by ELISA and low or undetectable neutralizing antibodies on the day of challenge but strong anamnestic antibody responses were observed following challenge. Interestingly, 2 of 3 animals in group A showed evidence of transient viremia and more stable CD4 counts following challenge as compared to the other immunized animals and to non-immunized controls. Thus, immunization with cell-associated SIVsmB7 did not provide sterilizing immunity against challenge with a highly pathogenic SIV strain but might have caused virus clearance later in infection.

A-2 ***In Vitro*** **IL-4, IL-10 Synthesis and Occurrence of Apoptosis During HIV-Infection.**

S. HERNANDEZ-COTT[1], M. IRIZARRY[1], S. SAAVEDRA[3], A.M. DIAZ[1], A.M. DEL LLANO[2], AND J.A. LAVERGNE[1]. Dept. of Microbiology, Sch. of Med[1]; Dept. of Biology, Humacao Campus[2], Univ. of PR; San Juan VA Hospital[3].

The loss of immune functions following infection with human immunodeficiency virus (HIV) may result from altered production of immunoregulatory cytokines such as interleukin-10 (IL-10) and IL-4. Imbalances in the network of these cytokines may trigger the immune system collapse caused by HIV. In addition, these cytokines may alter or be altered by nitric oxide (NO) synthesis and can be involved in a cell depletion process called apoptosis. This process has been proposed by some investigators to be the cause of lymphopenia in HIV individuals. In this study, we analyzed the presence of IL-4 and IL-10 in the supernatants of unstimulated and pokeweed-mitogen (PWM)-stimulated peripheral blood mononuclear cells (PBMC) from normal as well as HIV-infected individuals, after three days of culture. To assess this, we measured both cytokines using specific enzyme immunosorbent assays (ELISA). We report that the levels of IL-4 are undetectable in both unstimulated and PWM-stimulated PBMC from both experimental and control groups. Among 26 patients tested for IL-10 production, the following results were obtained: one patient did not produce IL-10 in either stimulated or unstimulated cultures; of the remaining 25 patients, 5 of them showed lower than normal levels of IL-10 in stimulated cultures, and 20 of them had similar or greater levels than normal values in their stimulated cultures. Regarding the development of apoptosis in PWM-stimulated cultures, 29% of the samples tested (18/63) resulted in higher than normal values of cell death as measured by flow cytometry. Our results suggest that HIV+ individuals show alterations in IL-10 production and support the hypothesis of the down-regulation of T_H1-driven cell mediated responses among HIV+ patients. Apoptosis, therefore, could be a consequence of such a cytokine imbalance. (Supported by NIH-RCMI 03051).

A-3 **The Potential of Nitric Oxide Inhibitors for the Prevention of Apoptosis in Cultured PBLs from HIV+ Patients.**

M. GARCIA[1], A.M. DEL LLANO[2], S. SAAVEDRA[3], AND J.A. LAVERGNE[1]. Dept. of Microbiol., Sch. of Medicine[1], Dept. of Biol., Humacao Campus[2]; Univ. of Puerto Rico and San Juan Veterans Hospital[3].

HIV-disease is a group of clinical symptoms caused by a retrovirus called human immunodeficiency virus (HIV). The phenomenon of apoptosis (Ao) observed in cultured PBLs from HIV+ subjects continues to gain relevance as an important factor contributing to the massive depletion of CD4+ T lymphocytes during HIV disease progression. Moreover, oxidative stress and nitric oxide (NO) have been identified as other mediators of apoptosis and may be additional mechanisms of CD4+ T cell depletion (del Llano et al., 1993). We have shown that NO-Monomethyl-L-Arginine Monoacetate (L-NMMA), a NO inhibitor markedly decreases the occurrence of Ao in PBLs of HIV+ subjects (Lavergne et al., 1995). Therefore, we have tested the potential of several additional NO inhibitors (NOIs) with different mechanisms of action (7-nitroindazole; 7-NI and dexamethasone; DEX) as preventive agents of *in vitro* Ao. PBLs isolated from twenty HIV+ patients were stimulated with different mitogens (phytohemaglutinin, PHA; pokeweed, PWM; jacalin, JAC; and lipopolysaccharide, LPS) and cultured with NOIs for three days. Resulting cultures were analyzed by flow cytometry and the percentages of apoptotic nuclei were determined. Results show that all PBL cultures from HIV+ subjects have higher percent values of Ao (unstimulated:43±18; LPS:56±17; PWM:55±14; JAC:49±19) than PBL cultures from normal subjects (unstim: 30±8; LPS:36±6; PWM:38±6; PHA:38±8; JAC:33±10; PHA:38±8). However, L-NMMA is an effective NOI (LPS:19±10; PWM:36±12; JAC: 9±5; PHA 49±13) in HIV+ subjects. Experiments with DEX show a high percentage of inhibition of Ao induced by JAC, LPS and PHA (71, 74 and 72% respectively). Only 42% inhibition of apoptosis induced by PWM was observed with the use of DEX. These experiments show that NOIs are effective in decreasing apoptosis in PBLs from HIV+ patients, in particular L-NMMA and DEX. Supported by RCMI-RR03051, CIDIC-RCM,UPR.

A-4 Tunicamycin Inhibits Endothelial Cell Proliferation and Differentiation *in vitro* by Inducing Apoptosis. JUAN A. MARTINEZ AND DIPAK K. BANERJEE, Dept. of Biochemistry, UPR, Sch. of Med., San Juan, PR 00936-5067

It has been shown earlier from our laboratory that amphomycin inhibited the proliferation of capillary endothelial cells from bovine adrenal medulla. Studies from other laboratories have subsequently shown that (i) inhibitors of hybrid and complex type oligosaccharides inhibited endothelial cell differentiation; and (ii) other glucosidase inhibitors prevented angiogenesis and the tumor growth as well. We have now used tunicamycin, blocker of GlcNAc2-PP-Dol synthesis to determine whether N-glycosylation is a pre-requisite for angiogenesis. We have used a capillary endothelial cell line from bovine adrenal medulla as a model. Flow cytometric analysis of synchronized cultures showed a doubling time of ~78 hours: ~36 hrs in G1, ~8 hrs in S and ~24 hrs in G2+M. Angiogenic responsiveness was assessed by observing changes in morphological parameters (i.e. cell number, viability and differentiation into capillary tube-like structures). Cell morphology and doubling time changed depending on serum concentration (cells doubled in 2.5 days with no differentiation in 10% serum, doubled in 3 days and differentiated in 2% serum and never doubled but differentiated after 1.5 days in 1% serum). Exposure to 2 µg/ml tunicamycin completely arrested cell proliferation and differentiation. Cell cycle analysis showed apoptosis induced after 36 hours in culture. We then concluded that N-glycosylation is an essential step for angiogenesis, probably serving as a checkpoint for cell cycle progression. Research support provided in part by the CIDIC grant.

A-5 **Profile of Intracellular Metabolism of 3TC**
Rafael A. Nieves, Hildamari Sánchez, Marianela Pérez, José F. Rodríguez. School of Medicine, Medical Sciences Campus, UPR.

3TC is a potent and selective inhibitor of HIV replication, an is currently in clinical trials for treatment of AIDS in children and adult alone and in combination with other antiretroviral drugs. Th metabolism of 3TC was studies in resting and stimulated peripher blood lymphocytes (PBMCs) as well as cord blood lymphocytes. A clinical relevant concentrations, 3TC was found to be anabolized to fiv different intracellular metabolites, similar to that found for ddC. Unlik AZT and other analogs, a limiting step in the phosphorylation of 3TC i the last step for the conversion of the diphosphate to the analo triphosphate, 3TCTP. The amount of 3TCMP formed in the PBMC was relatively low compared to the other phosphorylated produ indicating that the initial step of phosphorylation via deoxycytidin kinase is fairly efficient both in the resting and activated PBMC: However, resting PBMCs accumulated twice the level of the diphosphat analog compared to the triphosphate; stimulation of the PBMCs results in a shift in the profile and an increased accumulation of 3TCTP in th activated cells. These results suggest that 3TCDP may not b phosphorylated effectively to the triphosphate in PBMCs by NDPK an that the activity of the enyme responsible for this phosphorylation ma be dependent on the activation state of the cells. Since the intracellul half life of the triphosphate derivate of a nucleoside analog may be mor relevant to the persistence of antiviral activity than the serum eliminatio half life of the parent nucleoside in drug treated patients, the decay tim of 3TC triphosphate in PBMC cells was measured after removal of dru from medium. The measured half life of 3TCTP was 5.01 hrs for th activated cells and 8.42 hrs for the quiescent cells.

A-6 **Glutathione Plasma Concentration in HIV Infected Children**
Joel A. Cordero, Rafael E. Rueda, José F. Rodríguez. School of Medicine, Medical Sciences Campus, UPR.

Studies have demonstrated significant lowered concentration of glutathione in plasma, lung epithelial fluid, and T-lymphocytes in the adult population with human immunodeficiency virus (HIV). HIV replication may be potentiated by the decrease amount of glutatathione in cell and plasma. In addition, this glutathione deficiency can accelerate disease progression, especially in patient with increased levels of inflammatory cytokines, since the cytokines stimulates HIV replication more efficiently in glutathione depleted cells. The overall depression of the immune function is related with deficiency of normal concentration of glutathione. The mechanism for the depletion of glutathione in this patient population is still uncertain, thus the complete profile of the glutathione precursors could provide an insight into the possible mechanism of this depletion.

Several method have been employed for the quantitation of glutathione, including HPLC using electrochemical, ultra-violet, or precolumn derivatization-fluorescence detection. However non of this method profile of thiol constituents such as glutathione, cysteine, and cysteine-glycine. We present a simple relayble and fast method for the determination of this thiols compounds in plasma sample in less than 10 minutes. In addition, results from HIV infected Puerto Rican will be presented.

A-7 **Impaired Susceptibility to Activation-Induced Cell Death after CD3 Stimulation in a HIV-1 Chronically Infected T Cell Clone.** E. CRUZ[1], A.M. DEL LLANO[2], M. ANTOUN[3], AND J.A. LAVERGNE[1], Dept. Microbiol., Sch. Med.[1]; Dept. Biol., Humacao Campus[2], Dept. Pharm. Sciences, Sch. Pharmacy[3]; UPR.

Several reports suggest that activation-induced cell death is controlled by IL-2 (Lenardo et al. 1991 and 1993). In this report, we tested the hypothesis that exogenous administration of IL-2 to an IL-2 deficient T cell line will restore a pathway for apoptosis controlled by this cytokine after activation. We studied this effect on Jurkat and Jurkat-derived J1.1 clones. The HIV-1 chronically-infected J1.1 cell line has been reported to be defective in Ca^{2+} mobilization and IL-2 production after CD3 stimulation (Perez et al., 1991). In our experiments, IL-2 was added to all cultures at 100U/ml and stimulation with varying doses of immobilized anti-CD3 antibody (.1-6 µg/ml) was performed in a 3-day culture. Flow cytometry evaluation of cultures after propidium iodide staining of nuclei revealed that at low anti-CD3 antibody doses, both cell lines progress into proliferative states, a similar effect observed after stimulation with pokeweed and jacalin mitogens. However, at high anti-CD3 doses, Jurkat cells progress into S-phase followed by apoptosis (increased nuclei in the Ao stage of cell cycle, 26%), whilst J1.1 cells become arrested in S-phase but do not progress into apoptotic death (6% of cells in Ao). These results show that the activation-induced cell death (AICD) pathway mediated by IL-2 after anti-CD3 stimulation is deficient in J1.1 cells probably due to the integration of the HIV-1 genome. Furthermore, we evaluated the cell surface expression of Fas molecules (CD95) and found increased expression of this antigen in J1.1 cells (99% as compared to 58% in Jurkat cells). Experiments in

progress will evidence if the Fas-mediated death pathway is preserved in the J1.1 cell clone since previous reports have demonstrated an IL-2 dependent but cell-cycle-independent Fas regulation of AICD on activated T cells (Fournel et al., 1996). Supported by RCMI/RR03051; CIDIC-RCM, UPR; PR Cancer Center; PR Harris Fellowship.

A-8 **Fat and Breast Cancer in Puerto Rico: A Pilot Study**

Michael J. González, Emily Santiago, Cynthia Pérez. Nutrition Program; Departments of Human Development, Biostatistics & Epidemiology, School of Public Health, MSC.

A case-control study was conducted to examine the possible association between dietary fat intake and the development of postmenopausal breast cancer in patients attending the breast cancer clinic of the University Hospital in San Juan, P.R. Eighteen cases and eighteen controls were interviewed to obtain sociodemographic information, medical history and dietary fat intake. A semiquantitative food frequency questionnaire containing 67 food items was used to collect the dietary information. Estimates of relative risk showed a positive non-significant association for total fat intake and the development of postmenopausal breast cancer (OR = 1.57; 95% CI:0.42-5.90, p =0.25). The same non-significant association was found for saturated fat intake (OR = 1.57; 95% CI:0.42-5.90, p = 0.25). Polyunsaturated fat and monounsaturated fat were also positively associated with postmenopausal breast cancer, although the strength of the association was weaker (OR = 1.25; 95% CI:0.34-4.64, p = 0.37, for each one). Marital status and place of residence were found to be potential confounding variables, but adjusted odds ratios could not be calculated due to the small sample size. These results are consistent with other case-control sutdies that have shown non-significant positive associations between total fat and the different components of dietary fat and postmenopausal breast cancer.

A-9 **IL-1a and IL-6 Enhance the Co-Expression of IL-8 and GM-CSF Proinflammatory Cytokines and Growth of Human Head and Neck Squamous Cell Carcinomas.** Iris Colón*, Nerian Ortiz*, Z. Chen and C. Van Waes. NIDCD, NIH. *RCM, UPR.

Head and neck squamous cell carcinomas (HNSCC) can induce local and systemic changes in inflammation, angiogenesis and metabolism inpatients, and these changes have been associated with tumor growth and progression. Similar local and systemic responses are coordinated by cytokines that enhance the response and proliferation of cell in wounds following injury. To identify candidate factor(s) capable of modulating tumor growth and the local and systemic inflammatory responses that occur in response to these tumors, we characterized the expression and growth effects of regulatory cytokines produced by human HNSCC lines. HNSCC lines representing different sites and stages were screened for the expression of twelve regulatory cytokines by ELISA. HNSCC lines frequently secreted the cytokines IL-1a, IL-6, IL-8 and GM-CSF, which possess defined proinflammatory and angiogenic activity. The expression of the four cytokines by SCC cell lines often varied together, suggesting a pattern of coordination in expression. The variation in cytokine secretion correlated with differences in cytokine mRNA expression detected by Northern Blot and semi-quantitative RT-PCR analysis, providing evidence that the differences in secretion varied with steady-state mRNA expression. We determined whether IL-1a and IL-6, which participate in the regulation of expression of IL-8 and GM-CSF, contribute to the coordinated expression of these cytokines in HNSCC lines. Addition of Il-1A and IL-6 synergized to induce increased secretion of IL-8 and GM-CSF by the cell lines. Addition of IL-1 Receptor Antagonist or anti-IL-1 antibody partially inhibited secretion of IL-8 and GM-CSF. The increase in level of proinflammatory cytokines was associated with enhanced proliferation, while neutralization inhibited growth in MTT assay. Thus, we have identified a repertoire of cytokines that are co-expressed by HNSCC that may provide a growth advantage through direct as well as indirect effects mediated by proinflammatory and angiogenic responses. Evidence that IL-1a and IL-6 can enhance the co-expression of IL-8 and GM-CSF in SCC establishes the potential for autocrine or paracrine regulation of expression of these proinflammatory cytokines in SCC.(Supported by NIH)

A-10 Prevalence of positive results for illicit drugs in urine samples. ESTAPE E., BECERRA I., FIRPO A., College of Health Related Professions and School of Medicine, Medical Sciences Campus, University of Puerto Rico and Clendo Reference Laboratory

Efforts to deal with the problem of drug abuse include the collection and analysis of urine samples for the presence of the following illicit drugs: Cocaine (Coc), cannabinoids (cann), opiates (op), amphetamine (amph) and phencyclitine (PCP). We decided to examine the prevalence of these drugs in all consecutive urine samples received in a private reference clinical laboratory in Puerto Rico in the same month during three years. Samples were collected from the private sector, rehabilitation program and jail inmates at their time of confinement samples were processed according to an established chain of custody protocol and laboratory methods.

The total number of samples received for the same month for 1994, 1995 and 1996 were 972, 1169 and 1220 respectively. Review of the total positive results showed the presence of at least one drug of abuse in 34% of the samples in 1994, 32% in 1995 and 44% for 1996. The most abused drug used alone or combined was Coc. The prevalence of positive results for cann and op varied according to the mode of drug use: Cann for single and op for multiple use. An increase in the number of positives for op was noted in 1996 (23%), when compared to previous years (14 and 17% for 1994 and 1995). This increase was associated with a concurrent increase in the simultaneous use of coc and op, from a 68% in 1994 to 75% in 1996. This study suggests that the number of positive samples for illicit drugs, as well as multiple use of drugs, is increasing. This tendency is mainly noted in the group at confinement, such that this population should be included in studies evaluating patterns of drug abuse.

A-11 Paget's Disease of the Nipple-Areola Complex: Experience at Former UDH Radiation Oncology and Affiliated Institutions. H. Ortiz, I. Santiago, V. Marcial, J. Tomé, J. Ubiñas.

Mammary Paget's Disease is a rare entity described since 1856 and its histopathogenesis and treatment remains on discussion.

A review of the records of breast cancer patients over the last 25 yrs. reveals an incidence of this disease of approximately 1%. The age range was from 33 yrs. old (1 case) to 90 yrs. old (1 case); 86% of all cases were between 40 to 69 yrs. old.

Thirty-six percent were still with menses or early menopause (5 yrs. of less); 36% had long menopausal status (10 yrs. or more).

The most common symptoms were: a palpable breast mass by the patient, 41%; bleeding from nipple, 32%. In one case the first complaint was breast discomfort and, in another, burning sensation in the nipple. The initial clinical diagnostic impression of a

dermatological problem was done in 23% of cases. Receptors were done only in 6 patients (4 negatives and 2 positives). (In 64% of cases a tumor mass was demonstrated at diagnosis and an initial mammography was positive for cancer in 53% vs. negative in 47%. Seventy-three percent were infiltrating duct cell ca.; 8% in situ; and 14% intra ductal. Pathology of axillary nodes was positive in 64%, vs. negative in 36% of cases. Statistical correlations of these possible significance of prognostic variables will be done. As traditionally, 73% of patients were treated by radical modified mastectomy and radiotherapy as an adjuvant therapy, but 5 pts. have been treated lately by tumorectomy and radiotherapy as the main treatment.

On last follow-up (5 yrs. or less), 50% of the cases reveal no evidence of disease. There are 2 cases without relapse in 10 yrs. and 13 yrs. (conservative management).

Most common pattern of relapse was dissemination of the cancer. Cases with breast preservation have excellent cosmesis.

Source of funding: CIDIC

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ABSTRACTS

OB/GYN and Pediatrics

A-12 HORMONAL SCREEN OF HIRSUTE WOMEN IN A PUERTO RICAN POPULATION

T Diaz, G Perez, RI Cruz, J Romaguera, Department of Obstetrics and Gynecology, University of Puerto Rico, USA

Hirsutism in women is a manifestation of excessive production of androgens, the source of which can be the ovaries, the adrenals or increased peripheral conversion of weak androgens to more potent androgens. Distinguishing between the three sources is important because treatment should depend on the underlying disorder. In spite that hirsutism is not uncommon in Puerto Rico, we have no prior studies that deal with the differential diagnosis regarding our hirsute women. We performed ACTH stimulation and insulin tolerance test in 26 patients referred to us because of an hirsutism score of 10 or more. The hormones measured were total testosterone, free testosterone, sex hormone binding globulin, 17 hydroxyprogesterone, and dehydroepiandrosterone sulfate. We also determined the insulin and glucose levels. These tests could identify 21-hydroxylase deficient nonclassic adrenal hyperplasia, excess ovarian activity, adrenal disorders, or androgen producing tumors.The results from two patients (7.7 %) suggested subtle defects in adrenal steroid genesis. The rest (92.3%) most probably had a metabolic disorder of ovary leading to excess production of androgens. None of them presented androgen levels indicative of nonclassic congenital adrenal hyperplasia.

*This investigation was supported, in part, by a RCMI Clinical Research Infrastructure Initiative (RCRII) Award, 1P20 RR 11126, from the National Center for Research Resources, National Institute of Health.

A-13 Incidence of Intrauterine Fetal Demise Among a High Risk Population Followed with Intensive Fetal Monitoring

A. de la Vega, D. Vázquez. Department of Obstetrics and Gynecology, School of Medicine, MSC.

The stillbirth rate defined as those fetal deaths occurring after the 20 week of gestation has been reported to be 7.8-8.4/1000 births in the U.S. among the general population. It is expected that this rate would be much higher of a population identified as "high risk". We determined the incidence of stillbirths of 1450 high risk private patients delivered from January 1993 through February 1997. There were a total of 12 fetal deaths of 9 pregnancies giving a stillbirth rate of 8.2/1000 births. The average age at detection of fetal death was 29.1 weeks (range 20 to 37 weeks). The most common maternal condition associated with stillbirth was diabetes mellitus (44%). In only one case the fetal death remained unexplained and was not associated with any identifiable maternal or fetal risk factor. All these patients were part of a high risk population followed intensively throughout pregnancy with frequent sonography, biophysical profile determination, amniotic fluid analysis, and fetal heart rate studies. Although these data are of limited size, and therefore can not be used to draw definite conclusions, the fact that stillbirth rate among this high risk population was similar to that of the general population in the U.S., suggests that intensive fetal surveillance may have merit among this category of patients.

A-14 Incidence of Intrauterine Fetal Demise Among a High Risk Population Followed with Intensive Fetal Monitoring

A. de la Vega, D. Vázquez. Department of Obstetrics and Gynecology, School of Medicine, MSC.

The incidence of cesarean section among fetuses with unrecognized chromosomal abnormalities has been reported in the past to be as high as 50%. Because of the general increase in C.S. rates throughout the U.S. there is a need to reevaluate this relative frequency. We examined the incidence of fetal chromosomal anomalies among a high risk population followed at a private hospital in San Juan. There were 9 cases of chromosomal anomalies documented by karyotype analysis among the 1377 patients followed and delivered from January 1993 through February 1997 (.65%). Among this group, 5 cases were detected by a combination of maternal serum screening, analysis of risk factors and sonography. Among these, 3 patients elected pregnancy termination, one fetus with trisomy 21 was delivered stillborn at 32 weeks, and another with trisomy 18 was delivered alive at 29 weeks. Among the 4 cases not recognized prenatally, one fetus of trisomy 21 was delivered at 27 weeks by cesarean section due to malpresentation, and 3 cases (2 with trisomy 18 and one trisomy 21) were delivered by emergency cesarean section due to suspected fetal hypoxia. The very high relative frequency of emergency cesarean section (100%) among these cases should make us increase our efforts at the prenatal diagnosis of these conditions in order to avoid unnecessary surgical intervention.

A-15 Myometrial Performance of Teenage Patients

A. de la Vega, J. Rivera, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

Pregnancy in a teenage patient is known to be associated with increase in the relative frequency of preeclampsia, preterm delivery, and small for gestational age fetus, all of which appear to be a consequence of suboptimal development of the placenta in the hypoplastic and not well vascularized uterus of a teenager. Little attention has been given to the hypertrophy of the myometrium that has to occur during pregnancy, and the mechanical performance of this muscle during labor. The following ongoing study was designed to test the hypothesis that the uterus of the teenager with a relatively short menarche to labor interval (MLI) is functionally different from that of patients with longer (>4 yrs) menarche to labor interval. Our Department has about 8,000 deliveries per year of which 28% are teenagers (10 to 19 yrs). The relative frequency of cesarean section of patients with MLI of 4 years or less was 34% in contrast to 15% of the patient with MLI of 5 to 9 years ($P<0.01$). The former group also had a prolonged latent phase, less rapid cervical dilatation, but about the same length of second stage of labor in comparison to the group with longer MLI. Post partum uterine atony was also more frequent in patients with short MLI. We conclude that the myometrium of patients with short MLI has inferior performance characteristics than that with a longer MLI.

A-16 The Overlooked Surgical Margin

W. Torres, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

Proximity of invasive cancer to the margins of a surgical specimen is considered to be a good indicator of the probability of local persistence or recurrence of the neoplastic process. Traditionally a "surgical margin" denotes separation of tissues by transection with a sharp instrument ignoring the separation of tissue plains by blunt dissection. We examined the reports regarding surgical margins created by sharp or blunt dissection of radical hysterectomy specimens from the University Hospital from 1994 to 1996. We concentrated on the distance separating the tumor invading the cervical stroma from the anterior and posterior surface of the cervical body. The distance between tumor in the cervical stroma and the periphery of the cervical body in 83 percent of the cases was significantly less than the distance from tumor to transected walls of vagina, parametrial or paravaginal tissues (mean 8.8 mm v 19.6 mm). In some specimens the tumor was separated from the periphery of cervix by a few mm of normal tissue only. In all of the reports margins of resection were described as free of tumor. We propose a redefinition of the term "surgical margin" of specimens with invasive carcinoma by including plains created by blunt dissection. This would reflect more precisely the risk of residual microscopic tumor in the muscularis of the bladder.

A-17 Reasons for the Ineffectiveness of Propranolol to Resolve Arrest of Labor

N. Rodríguez, R. Burgos, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

We have demonstrated previously that about 70% of patients in arrested labor refractory to oxytocin, will deliver vaginally following 2 mg of propranolol. The success rate was even higher among patients classified as hyperadrenergic. However, even in this population there were patients in whom full dilatation of cervix could not be achieved. In our previous studies we had not paid attention to the position of fetal head at the time of arrest. Since in a primigravida descent of fetal head below 0 station is often necessary to achieve full cervical dilatation, occiput posterior position (OP) might explain the failure of propranolol treatment. The following case supports such a contention. A 19 y, g 1 at 37 weeks of gestation was admitted in active labor with cervical dilatation of 3 cm at station -1. She progressed to 8 cm from which neither cervical dilatation nor station of the presenting part changed for the next 2 hours in spite of regular contractions augmented with oxytocin. Because of a family history of hypertension, she was given 2 mg of propranolol. There was no progress over the next 2 hours, and she had to be delivered by cesarean section. The fetus was found to be in OP position at 0 station. We suggest that positions which prevent descent are responsible for the failure of propranolol to achieve vaginal delivery in patients without CPD. We are reviewing our failed propranolol treated cases to determine whether the fetuses were in OP position. If this is found to be true, propranolol will not be recommended in such cases.

A-18 The Limits of Routine Obstetric Ultrasound

A. de la Vega, D. Vázquez. Department of Obstetrics and Gynecology, School of Medicine, MSC.

Routine prenatal sonographic evaluation of the fetus for the detection of fetal anomalies is an almost universal practice among private and public prenatal care services in Puerto Rico. In view of the popularity of this evaluation technic we must be acutely aware of the sensitivity, and specificity that this methology provides. We examined the diagnostic accuracy of routine obstetric sonography in a private obstetric population consisting of 1357 patients delivered between January 1993 and February 1997. In all cases the sonographic examination was performed by two experienced physicians with no limits set regarding the number of sonograms performed. A total of 29 fetal anomalies were detected at birth (incidence of 2.1 %). Of these, only 20 cases had been diagnosed prenatally, There were no cases of false positives. The sensitivity of this test was 68.9%, specificity 100%, positive predictive value 100%, and negative predictive value 99.3%. We call attention that although sonography equipment and our skills have improved greatly over the last few years, this methology has its limitations regarding sensitivity, and therefore both the physician and the patient must be aware that even repeated negative sonograms do not guarantee absence of fetal anomalies.

A-19 Sonographic Findings in Two Cases of Prenatally Detected Müllerian Tract Anomalies

A. de la Vega. Department of Obstetrics and Gynecology, School of Medicine, MSC.

Severe Müllerian defects are infrequently diagnosed prenatally since in most cases they will show no clinical signs until after puberty. However, in cases where the Müllerian anomaly is associated with urinary tract abnormality, the Müllerian tract anomaly might be detectable. We present two cases of prenatally diagnosed genitourinary anomalies in which a communication existed between ureters and uterus combined with an obstructed vaginal tract. In both cases polyhydramnios, ascites and an abdominopelvic cystic mass localized posterior to the fetal bladder was present. In one of the cases esophageal atresia was also present which was diagnosed postnatally. In both cases karyotype analyses was normal. Both of these cases had come to our service with a diagnostic impression of a fetal gastrointestinal obstruction. We present these findings as a reminder that although rare, this condition should be included in the differential diagnosis of a fetal abdominopelvic mass.

A-20 Hemoglobin S Haplotypes in Puerto Rican Children with Sickle Cell Trait.

P.J. Santiago-Borrero, C. L. Cadilla, A. E. Rodríguez, E. Rivera-Caragol and G. Rivera. Department of Pediatrics, Biochemistry and Microbiology, UPR MSC School of Medicine.

Sickle Cell Disease (SCD) has been related to five principal Beta S (β^S) Haplotypes, namely: #19 (Benin), #20 (Bantu), #17 (Cameroon), #3 (Senegal) ; and #31 (Saudi Arabian), which is almost indistinguishable from #3. Some SCD patients fail to

show any of the reported mutations or present atypical haplotypes. Twenty eight (28) Puerto Rican individuals with sickle cell trait, including 23 newborns, were studied for β^S haplotypes. Gamma A ($^A\gamma$ promoter and $^A\gamma^T$), and gamma G ($^G\gamma$ promoter) regions were examined using PCR amplification, and Southern Blot hybridizations with allele-specific oligonucleotide (ASO) probes. Only 16 (57%) of the 28 sickle cell trait individuals showed the reported typical African β^S haplotypes. Eleven (39%) showed an unusual mixture of mutations, that often were compatible with 2 or more common haplotypes. The mutations found in the persons studied included: #20 (57%), #19 (50%), variable mixed mutations (39%), #3 (18%) and #17 (14%). These allele frequencies are different from those found among patients with symptomatic sickling syndromes. Some chromosomes in normal individuals (Beta A, β^A genes), contained mutations similar to those recognized in Beta S globin. It is likely that a fraction of the mixed mutations seen in these persons came from the normal β^A present in indivuals with the sickle cell trait. (Partially supported by Project MCJ-72100503-0, the UPR-MSC CIDIC Program of the Deanship of Academic Affairs and a Research Centers in Minority Institutions Award, G12RR-03051, from the National Center for Research Resources, National Institutes of Health.

A-21 **Chemotherapy During Pregnancy and its Effects in the Fetus: Neonatal Myelosuppression -2 Cases Report**

L García, M. Valcárcel, P. J. Santiago Borrero; Department of Pediatrics, Neonatology and Hematology Sections, UPR School of Medicine

Leukemia during pregnancy is not a frequent event. Most of the cases are diagnosed during prenatal visits. It presents an ethical dilemma since it is known that with effective chemotherapy complete remission can be obtained in up to 75% of patients, but it is also known that chemotherapy has potential harmful effects to the fetus. We present a 21 y/o female diagnosed with acute myelogenous leukemia during pregnancy and who was given chemotherapy starting at 21 weeks gestation. She received three courses of chemotherapy which included cytarabine, daunorubicin and Mitoxantrone. She gave birth to a single preterm female baby after 29 3/7 weeks of gestation by Cesarean section. Birth weigth was 0.857 kg. Initial laboratories showed severe neutropenia, anemia, and thrombocytopenia. Bone marrow aspiration showed complete marrow aplasia. She was treated with blood product transfusions, erythropoietin and granulocyte colony stimulating factor. After 12 days of therapy, the hematologic derangement was resolved. No infections were documented. The second case was a 30 y/o female diagnosed with malignant lymphoma and treated with chemotherapy since 28 weeks gestation. She was treated with cyclophosphamide, doxorubicin, vincristine, and prednisone. She gave birth to a single preterm male baby after 33 weeks of gestation, with a birth weight of 1.645 kg. He presented with leukopenia without neutropenia which lasted for 2 days. Platelet counts and hemoglobin were normal. He had an uneventful course and was discharged home after 10 days, without documented infection. Exposure of the fetus to transplacental chemotherapy must be considered when deciding therapy as well as timing of delivery in hematologic malignancies diagnosed during pregnancy.

A-22 Profile of a High Risk Adolescent Population

B. Mirabal, H. De Jesús, J. MOntilla, A. Matos, M.N. De Jesús, N. Vázquez. Dept . of Pediatrics, School of Medicine and School of Nursing, UPR Medical Sciences Campus

In response to the high prevalence of adolescent mothers in Carolina (15.6% of live births) and the alarming number of active child protection cases in PR (over 48,000 in 1994-95)the Biopsychosocial Program of the Dept. of Pediatrics developed the "Community Project in Support of Adolescent Mothers" in collaboration with the school of Nursing and the PR Dept. of FAmily Services. The main objectives were 1) prevent child abuse in infants of these adolescent mothers and 2) Develop a support system for them by community networking. These results represent a profile of this population which will help to develop guidelines for effective preventive measures. 32 pregnant adolescents were recruited in the 3rd. trimester from the Carolina LHC Adolescent OB-Gyn clinic. After a written consent, the adolescents filled out a profile and needs assesment. Weekly psychoeducational group sessions focused on parenting skills, began prior to delivery and continued for 10 months. At least one home visit/adolescent was performed. Mean age of adolescents was 17.2 years ±1.6; median age of 17.0 yrs. (range= 14-19 yrs.).22% had completed high schools; 45% only had a ninth grade. 30% still in school. 39% were married; 29% lived consensually. 40% had one or more previous pregnancies; 31% had ± 1 child. 87% were medically indigent. Currently 31% attend sessions regularly. No child abuse has been detected. Results suggest preventive, educational efforts geared towards this population must be accessible and innovative; an intensive home visiting program is strongly recommended.

A-23 **Consequence for Having Accepted the Erroneous Hypothesis of a Spherical Alveolus**

R. George, K. Adamsons. Department of Obstetrics and Gynecolosy, School of Medicine, MSC.

Unlike earlier in this century when much of scientific communications dealt with the examination of proposed concepts or hypotheses, our present reports deal mainly with the statistical analysis of our observations. There appears to be a responsibility of the scientific community, however, to allocate time to the examination of previously accepted concepts which are incompatible with reality, particularly when such concepts influence the direction of our present research and even our clinical practice. The spherical alveolus is one such example. Introduced into our literature in the middle of this century, it forced the student to assume that breathing necessitated the stretching of the walls of the alveolus, when in reality the volume of the alveolus is changed by changing the angle between intercepting surfaces. We were further requested to accept that the stretching process required the presence of surface tension reducing substances. A major scientific effort has been expended in this area of inquiry, hoping to resolve ventilatory problems of the preterm infant. What is difficult to understand is that the idea of the spherical alveolus was accepted in spite of the fact that nobody had seen such a geometric structure in the preparations of the lung. The specific density of the inflated lung of about 0.16 is too low to be compatible with a spherical model. Furthermore, an expanding spherical alveolus would have

to expand also the interalveolar spaces requiring an increase of mass of lung during inspiration. There should be no hesitancy to dismiss this erroneous hypothesis, and to reexamine the role of surface tension reducing substances in the function of lung.

A-24 Normal Hand Anatomy of a Fetus with Choroid Plexus Cysts and Trisomy 18: Do Not Rely Too Much on Sonography

A. de la Vega, D. Vázquez, L. Lynch. Department of Obstetrics and Gynecology, School of Medicine, MSC.

The presence of choroid plexus cysts has been associated with trisomy 18, particularly if other anomalies are detected. However, the issue of whether fetal karyotyping is indicated in cases of isolated choroid plexus cysts is highly controversial. Most neonates with trisomy 18 have abnormal hand positioning or hand anomalies. Therefore, some authors have suggested that normal hands at the time of ultrasound rules out the possibility of trisomy 18, and these patients should not be offered amniocentesis. We present a case of "isolated" bilateral choroid plexus cysts with trisomy 18 documented by karyotype analysis in which the fetal hands were evaluated by ultrasound and found to be normal with normal positioning of the fingers at 18 weeks of gestation. Pathologic evaluation after pregnancy termination confirmed these impressions. No anomalies were detected in this case except for bilateral choroid plexus cysts. The abnormal hand positioning seen in trisomy 18 develops over time as a result of neurological impairment. Therefore the sensitivity of hand examination for trisomy 18 should be inversely correlated with gestational age at the time of ultrasound evaluation. The absence of findings in this case should remind us that sonography is of limited sensitivity in the diagnosis of chromosomal abnormalities, especially during the second trimester.

A-25 Nonresponsiveness of Lecithin Sphingomyelin Ratio of Amniotic Fluid to Glucocorticoid Therapy

J. Romaguera, L. Lynch, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

Appearance of various phospholipids in amniotic fluid correlates well with the function maturity of the lung of preterm infant. The purpose of this prospective, double blinded, randomized study was to compare the effect of dexamethasone administration to the mother (6 mg q 12 hrs x 4), considered by many to be an effective accelerator of fetal maturation, with that of dexamethasone treatment of the mother, but combined with intraamniotic administration of thyroxine (500 micrograms). The L-S ratio was chosen as the indicator of maturity of lung. We report the analysis of the first 76 patients enrolled in the study. Arrested preterm labor was the indicator for acceleration of fetal maturation in both groups. Fetal age at the initiation of the treatment ranged between 24 to 31 weeks. The slope of the L-S ratio curve one week after dexamethasone administration alone was 0.20 in contrast to 0.65 for the group receiving dexamethasone to the mother and thyroxine intraamniotically ($p<0.05$, t-test for independent samples). The slope value for the group receiving dexamethasone alone was similar to that of our previous study group without any prenatal treatment. We conclude that glucocorticoid plus intraamniotic thyroxine accelerates the progression of L-S ratio of amniotic fluid of a preterm fetus, as compared to no change in the group who received only glucocorticoids.

A-26 Menarche to Conception Interval as Predictor of Preeclampsia in Teenage Patients

J. Rivera, A. de Jesús, A. Avilés, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

We have proposed that preeclampsia is caused by yet to be identified substances released by the trophoblast when the PO2 of that tissue falls below 30 torr. In support of this hypothesis we have consistently found a low PO2 in the umbilical vein (by cordocentesis) of patients with preeclampsia, and have observed a lowering of systolic and diastolic BP when the PO2 of the intervillous space was normalized by increasing the fluidity of maternal blood by the administration of albumin. Thus the cause of preeclampsia of a teenage patient should be the restricted growth of placenta in a hypoplastic uterus. This in turn is expected to be a function of the preconceptual estrogenization of the uterus, determined by the interval between menarche and placentation (MPI), rather than that of the chronologic age of the patient. To test this hypothesis we analyzed the relative frequency of preeclampsia in our teenage population (28% of our delivery census of about 8,000 patients per year) as a function of MPI. The relative frequency of preeclampsia was 24% in patients with MPI of 4 years or less. In contrast, no teenager with a MPI of 5 years or more had preeclampsia, unless the patient prior to conception had been on low estrogen contraceptives. We conclude that a teenage patient with a MPI of 5 years or more has lower risk for developing preeclampsia than our general obstetric population.

A-27 Potential Risk of Alpha Adrenergic Blockade in Preeclampsia

I. Colón, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

Vasoconstriction of cerebral vessels has been considered as a cause of CNS abnormalities in preeclampsia and eclampsia. No attention appears to have been given to the interpretation that vasoconstriction is a response to protect intracranial circulation, particularly the subarachnoid vessels, from high distension forces. It is not known whether the proposed protective mechanism depends on adrenergic receptors or other mediators. If alpha adrenergic receptors were involved, administration of alpha blocking agents could weaken the protection of cerebral vessels. The following case report endorses such a hypothesis for causation of intracranial hemorrhage in preeclampsia. A 23 year old G2 P0 at 30 weeks of gestation was admitted from a private hospital because of preeclampsia. Prior to transfer, she had received an antihypertensive medication IV , which later was identified as labetalol. Generalized edema and BP of 170/110 were the only abnormal findings. After the administration of 25g of albumin, which lowered the blood pressure to 160/105, patient was given

20mg of labetalol IV. Within 10 minutes after the injection the patient became disoriented, and 20 minutes later became unconscious. Massive subarachnoid hemorrhage was demonstrated on CT scan. The systolic BP never rose above 160 torr. Her condition deteriorated progressively, and she was declared brain dead 45 hours later. We raise the question of the safety of antihypertensive agents with alpha adrenergic blocking properties in the treatment of preeclampsia, and have initiated studies in the Rhesus monkey to evaluate the impact of alpha adrenergic blockade upon cerebral circulation in the presence of increased inotropism.

A-28 Propranolol in the Management of Dysfunctional Labor

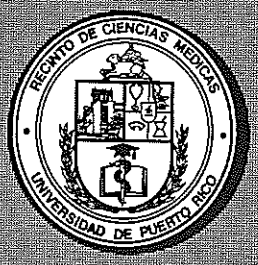
M. Flores, O. Sánchez, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

We have demonstrated previously that administration of propranolol to pregnant patients with arrest of labor of two hours or more, causes resumption of cervical dilation, and vaginal delivery is achieved in about 2/3 of patients who otherwise would have been delivered by cesarean section. The proposed mechanism of action is blockade of beta-receptors of myometrial cells, thus preventing the inhibitory effect of epinephrine. We are currently evaluating the usefulness of propranolol 1 to 2 mg i.v. in patients with slow progression of cervical dilatation, defined as less than 1.5 cm per hour in multiparous patients, and 1.2 cm per hour in nulliparous patients. Inclusion criteria call for identification of patients as "hyperadrenergic" on the basis of extreme anxiety during labor, or personal or family history of hypertension, absence of disproportion, and absence of malposition. Our ongoing study has revealed a consistent shortening of the active phase of labor in most patients, decrease in the use of analgesics, and better cooperation during the expulsive phase. We conclude that beta adrenergic blockade is a valuable addition in the conduct of labor in the hyperadrenergic patient.

A-29 Corticosteroid Pulse Producing Labor and Delivery Near Term

E. Muñiz, K. Adamsons. Department of Obstetrics and Gynecology, School of Medicine, MSC.

The reintroduction of glucocorticoids to accelerate fetal maturation in 1994 has resulted in the identification of such treatment as standard of care in cases of expected preterm delivery. Contrary to expectations this treatment has not reduced in larger studies the relative frequency of RDS of premature babies. The explanation might be that only in some patients glucocorticoids increase uterine activity thereby accelerating endogenous fetal maturation. In the sheep glucocorticoids are more potent than oxytocin to bring about delivery prior to term. Little attention has been paid to changes in the uterine activity after administration of glucocorticoids to accelerate fetal maturation in the human. The following case demonstrates the effectiveness of these compounds to initiate labor in preterm gestation. A 22 y, g 3, para 1 with multiple sclerosis was admitted at 36 weeks because of exacerbation of symptoms. She had no uterine irritability. Cervix was long and closed. Treatment with methylprednisolone 250 mg iv q 6 hours for 72 hours was initiated. This resulted in significant improvement of her condition. At the end of the 72 hours patient began experiencing uterine contractions. Cervix was found 2 cm dilated. She progressed rapidly and 2.5 hours later delivered a 2809 g male with Apgar score of 7-8. We propose that the mechanism for accelerating fetal maturation with glucocorticoids may lie in the endogenous release of TRH and other tropic hormones in response to fluctuation of fetal oxygenation caused by uterine contractions. Since homo sapiens is not a consistent responder to glucocorticoids regarding myometrial activity, this might explain the variable findings regarding acceleration of fetal maturation under steroid therapy.



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ABSTRACTS

College of Health-Related Professions

A-30 Conductas de riesgo en los adolescentes que impactan su vida futura: Proyección a estudiantes universitarios.

Ed.D., MPHE L. Soto de Laurido

La Encuesta de Conducta de Riesgo en Adolescentes, se realiza a nivel de la nación americana en todos sus estados, lo que incluye a Puerto Rico. Su objetivo principal es determinar cuáles son las conductas de riesgo de los adolecentes que se constituyen en las principales causas de muerte, morbilidad y problemas sociales en estos y en su vida adulta. Los datos responden a la recopilación que se efectuó de febrero a marzo de 1995. La selección de la muestra fue al azar con participación representativa de los estudiantes matriculados en las escuelas públicas de la isla. Específicamente de 9no. a 12mo. grado. Entre los resultados se destaca: un 35% de actividad sexual, un incremento en el uso de marihuana, de un 80 a un 90% de los estudiantes reportan haber recibido información en las escuelas sobre VIH/SIDA, como información de algunas de las categorías. Se concluye que los adolescentes llevan a cabo prácticas de riesgo que afectarán inevitablemente su vida actual y futura. Se justifica la creación de más programas de promoción de la salud y prevención de enfermedades crónicas.

A-31 Interdisciplinary Project of Excellence in Services

Font Rivera, Ana
PIES, College of Health Related Professions

The Interdisciplinary Project of Excellence in Services offers physical therapy, occupational therapy, speech and language pathology, psychology and evaluation in audiology and neurology to children with disabilities referred by the Special Education Program the Department of Education. The most common conditions treated in the Project are: cerebral palsy, attention deficit disorders, Down Syndrome, specific learning problems and mental retardation.

The Project has a training component for teachers, parents and health-related professionals on collaborative team work in the management of the client with developmental disabilities. This presentation will cover the specific principles and interdisciplinary activities of the Project.

A-32 Word form therapy in anomia: a case study

González, Ana and V. Marrero
Speech-Language Pathology - College of Health Related Professions

In recent years, numerous studies have been published examining the effectiveness of particular tasks in promoting word retrieval. Semantic and phonological tasks have been used alone or combined with a variety of experimental paradigms and subjects. These studies have left us with a need to know which procedures work best with particular patients.

The purpose of this study is to explore the efficiency of word form therapy in enhancing word retrieval in Spanish speakers with anomia.

Method: Our subject is a 63 year old male with Wernicke's aphasia. He is three years post onset and has 12 years of schoolings.
Procedure: Our subject was screened for verbal apraxia, hearing deficit and visual neglect. All three were ruled out. He was administered a naming test to ascertain whether he had knowledge of word form which he did. Traditional therapy consisted of confrontation naming with semantic, sentence completion and phonemic cues. Word form therapy consisted of confrontation naming with syllable blocks, letter blocks and letter form configuration.
Findings: Syllable block elicited word recall 100% of the time followed by semantic (traditional) cueing with a recall rate of 95%. Letter blocks elicited recall with 50% accuracy and letter form configurations did not elicit recall. It is concluded that visual information did not help this, patient recall words but kinesthetic cues such as block handling dit.
Further study: We need to further explore the impact of visual us tactile stimulations in patients with lesions different than this patients

A-33 Promoting changes in public school services for poor students at-risk for delinquency

Rivera, Edgar R. - Research and Projects Development Office - College of Health Related Professions

This project's main objective is to identify, promote and establish in-school services that will result in developing physical, mental, social, and academically healthy children, who in turn will be come transforming agents in their communities. The needs of the school community were evaluated through direct meetings with all its components and written evaluations performed by school personnel. Based on the needs identified interpersonal skills trainings were offered to the faculty.

Speech-language and occupational therapies have been offered to selected students. As identified through an informal evaluation performed recently by the school's faculty, the workshops are facilitating the development of a positive team spirit among them, and students love and enjoy the therapies. According to concerned teachers change is not evident in the children yet. In the second phase, the service needs identified will be dealt with through the coordinated efforts of a wide scope of professionals working as a team to provide students with integrated in-school services. The effect of these will be constantly monitored and adjusted as need. Preliminary results of the children's characteristics and the school environment will be presented.

A-34 Impacts of training and services on childhood autism

Jiménez, Rovira, Rentas & Linares
College of Health Related Professions

The Infantile Autism Project (IAP) main components are investigation, orientation and community service pertaining to the autistic population in P.R. We are working on the implementation of a school-based pre school model for autistic children, the training of speech language pathologists in the area of autism and the diagnosis of Autism islandwide. The impact of the IAP work is evaluated through data of children's progress, number of diagnostic evaluations, and the involvement of trained speech-language pathologists in the treatment of children with autism. Data on outcomes will be presented. This project is funded by the Department of Education (US & PR) and Puerto Rico Legislature.

A-35 Sensory functioning in children with autism

Jiménez, Rovira, & Rentas
College of Health Related Professions

Children with the autism sindrome seem to have abnormal responses to sensory input. It is theorized that most bizarre and abnormal behaviors seen in this population is related to abnormal processing of sensory input. In our work as part of the IAP diagnostic team we have seen youngsters with autism that show signs of sensory integrative difficulties. We theorize that the greater the sensory problem, the greater the severeness of the autism. A sensory guide was designed to describe behaviors that could be related to sensory problems in the vestibular, olfactory/gustatory, auditive, tactile, visual & proprioceptive areas. Problems are described as: severe, moderate or mild in two kind of responses (hyper or hypo). We compared these results with the level of autism as seen in the Childhood Autism Rating Scale.

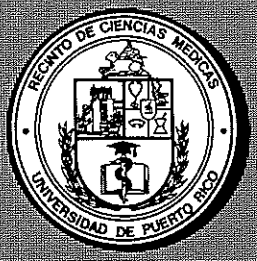
We found that, although the overall results indicated that there were no significant differences in the presence of sensory integrative difficulties in all three levels of autistic children, the severeness of the sensory integrative difficulty related to the severeness of the autism.

A-36 Transition for 6th Grade Public School Students at Risk for Delinquency, Cintrón, Mercedes- Ph.D.

Research and Project Development Office
College of Health Related Professions

This Project is based on research that suggests a decrease in motivation and increase in misconduct associated with transition to junior high school as a result of a mismatch between needs of developing adolescents and the opportunity afforded them by their school and families. The program is aimed at optimizing the conditions for successful transition for students identified at-risk for delinquency. Workshops are aimed at enhancing social skills and developing a support network between 6th graders, their 7th grade teachers and students from the new school. Additional community support comes from older adolescent of similar socio-economic background, graduates from youth leadership programs. First contacts, evidenced shared fears between incoming students and receiving teachers. Opportunity is set for fears to be shared and overcomed. Separate workshop for teachers explore practical ways of reducing the gap between adolescents needs and school environment. Participant's adjutment to 7th grade transition will be assessed and compared to a control group.

The Project has a training component for teachers, parents and health-related professionals on collaborative team work in the management of the client with developmental disabilities. This presentation will cover the specific principles and interdisciplinary activities of the Project.



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ABSTRACTS

Anatomy and Institute of Neurobiology

A-37 **Altered Levels of Sodium Pump in Vascular Tissues of Hypertensive Rats: A Longitudinal Study of the SJH-Rs Rat.** L. DIAZ, C. RODRIGUEZ-SARGENT AND S.C. COREY. Department of Pharmacology and Institute of Neurobiology, UPR-RCM, San Juan, Puerto Rico.

Levels of Na Pump α2 are significantly reduced in vascular tissues of rats with both spontaneous and experimentally-induced hypertension, supporting the idea that regulation of intracellular Na^+ plays a key role in the biogenesis of hypertension. To gain insight into the onset of hypertension, Na pump expression was studied in newborn salt-sensitive hypertensive rat SJH-Rs. Mothers of both SJH and control MW rats were fed the same high-salt diet (8% NaCl). Blood pressure was 140-240 mm Hg in SJH mothers, and 100-140 in the MW normotensive mothers. Levels of the three Na pump isoforms were determined in heart and kidneys using quantitative immunoblot analysis. The α2 isoform is not present in the neonatal heart, but its neonatal analog, α3, was found to be significantly elevated 157% in SJH neonates. The α1 isoform was unchanged in both heart and kidney. Relative renal weight, but not cardiac weight, was significantly reduced in SJH neonates. These data demonstrate that altered Na Pump expression from an early age in the SJH rat, indicating a defect in developmental regulation. Moreover, the data suggest that the tendency to develop salt-sensitive hypertension may be detectable at a young age. [Supported in part by the Fundacion Doctor Garcia-Rinaldi.]

A-38 **Identification of Peptidergic Neurons Involved in the Regulation of Feeding Behavior in Bursatella leachii.** MILLER, M.W.[1], SUAREZ, J.-C.[1], and TEYKE, T.[2]. [1]Inst. of Neurobiol. and Dept. of Anatomy, UPR RCM; [2]Inst. für Zool., J. Gutenberg Univ., Mainz, Germany.

The behavior of many animals, including humans, is said to be 'motivated' when its occurrence depends upon the presence of both extrinsic factors (e.g. the presence of food, a mate, a drug of abuse) and intrinsic variables (e.g. drive state, satiety level, or 'craving'). In certain molluscs, it is often possible to relate specific biophysical or synaptic properties of large identified neurons directly to the behavior of the organism. One opisthobranch mollusc that is indigenous to Puerto Rico, Bursatella leachii (the "ragged" sea hare), exhibits a number of properties that render it particularly suitable for examining the role of identified peptidergic neurons in the generation of motivated or goal-directed behaviors. In this study, standard electrophysiological (intra- and extracellular recording) and histological (immunohistochemistry, nerve backfill) methods were used to examine biting and locomotion, i.e. two behaviors that are co-active during feeding. In these experiments: (1) the rhythmic buccal and pedal central pattern generators associated with feeding were found to persist in the isolated Bursatella nervous system, (2) 'backfills' of the cerebral-buccal connective (CBC) were used to locate neurons in the cerebral ganglion that may act as command or modulatory elements in the regulation of biting, (3) backfills of the CBC toward the buccal ganglion revealed the locations of cells that may serve to provide a 'read out' or efference copy of the buccal motor program, (4) wholemount immunohistochemical methods were used to locate neurons in the buccal and cerebral ganglia that express a certain family of neuropeptides (the myomodulins) that are known to be involved in the regulation of feeding in molluscs, (5) identification of buccal neurons was initiated using dye (Lucifer yellow) injection in conjunction with intra- and extracellular recording. Supported by RCMI Award G12RR-03051 (NIH) and Puerto Rico EPSCoR.

A-39 Masses in the Third and Lateral Ventricles O. DE JESUS, B. NEGRON
Section of Neurosurgery, University of Puerto Rico

Masses in the third and lateral ventricles are uncommon, therefore, only small series had been reported. A large series is presented and reviewed according to epidemiology, presentation, localization, surgical procedure, and biological behavior. Thirty-eight patients with intraventricular masses diagnosed and managed at our hospital during a seven-year period were studied retrospectively. There were 16 pediatric cases and 22 adult cases. The most frequent neoplasm was oligodendroglioma. Arteriovenous malformations were the most common non-neoplasic lesions. Headache secondary to increased intracranial pressure was the most common symptom. Masses were most commonly found in the lateral ventricles except colloid cysts and craniopharyngiomas. The lateral ventricle was mainly approach through a frontal transcortical route or an anterior transcallosal route. The third ventricle was mainly approach through the lamina terminalis. Masses in the lateral ventricles were resected subtotally in 61% of the times, while those in the third ventricle were resected subtotally in 25% of the times. Those masses involving both locations were resected subtotally in 75% of the times. Sixty-three percent of the patients presented with hydrocephalus. Forty-one percent of them required a shunt before their major surgery, while 23% required it subsequently. There was no surgical mortality in this series. Postoperative seizures occurred in 37% of the patients, always associated to a transcortical approach. Neoplasms received radiation therapy 59% of the times and chemotherapy 14% of the times.
Conclusions: Treatment options depend on the location of the mass. Masses involving the lateral ventricles are usually resected subtotally. Recurrence is more common in pediatric cases. Postoperative seizures are associated to transcallosal surgery. One third of the patients with hydrocephalus never require a shunt. Chemotherapy is reserved primarily for pediatric cases in which radiation therapy could not be given.

A-40 NATURALLY OCCURRING MUSCULOSKELETAL DISEASES OF AGING NONHUMAN PRIMATES.

M.J. Kessler and K.P.H. Pritzker. Caribbean Primate Research Center, Medical Sciences Campus and Department of Pathology, School of Medicine, University of Puerto Rico, Sabana Seca, PR 00952-1053; Department of Pathology and Laboratory Medicine, Mt. Sinai Hospital, University of Toronto, Toronto, Canada M5G 1X5

Amongst primate species, there is widespread variation in body mass, body proportion and locomotive biomechanics. Notwithstanding the major differences in functional morphology and scale, the growth, maturation, composition, metabolism, and biomechanical properties of nonhuman primate musculoskeletal tissues closely resembles those of humans. Further, these similarities exist despite profound differences in habitat, diet and locomotor behavior. Thus, it is not surprising that nonhuman primates are subject to naturally occurring musculoskeletal diseases similar to humans and that experimentally induced musculoskeletal diseases in nonhuman primates resemble natural diseases of humans exposed to similar pathogenic agents. This presentation gives an overview of the major naturally occurring musculoskeletal diseases of aging nonhuman primates including arthritis [osteoarthritis, calcium pyrophosphate dihydrate (CPPD) crystal arthropathy, spondyloarthropathy] and osteoporosis. (Supported in part by NIH grant RR3640 and The Arthritis Society of Canada.)

A-41 Surgical Sterilization as a Means of Population Control for a Free-Ranging Introduced Primate Population in Southwestern Puerto Rico.

Janis González Martinez, Ph.D., Matt J. Kessler, D.V.M. Caribbean Primate Research Center, University of Puerto Rico-Medical Sciences Campus

Introduced populations of rhesus macaques (*Macaca mulatta*), and patas monkeys (*Erythrocebus patas*) have been free-ranging on the mainland of southwestern Puerto Rico for more than 30 years. The total number of both species of free-ranging monkeys is approximately 200-250 individuals. Both species could become very serious pests if their numbers increase or their distributions expand. While complete eradication of the monkeys is not likely to be possible in the short-term, with consistent measures over the long-term, eradication may be possible. We present a research plan to prevent the dispersal and expansion of the monkey populations, and eventually reduce the size of the populations. Our hypothesis is that surgical sterilization will diminish population growth, while retaining social structure and thereby limit population expansion. The reproductive output of this population can be regulated by trapping sexually active females, sterilizing them using a method which does not alter their social behavior, and releasing them back to their former social spaces in the population. We propose to use surgical sterilization by tubal ligation and vasectomy as means of population control. These methods have the advantage of guaranteeing contraception. Furthermore, by leaving the gonads intact it also has the advantage of having minimal effects on behavior. Reproductive productivity will be even further reduced by removing younger individuals via trapping. This will cause a shift in the age structure of the population in favor of older, less productive individuals with shorter, less productive reproductive life spans ahead of them, leading to a relatively more senescent, unproductive population.

A-42 THE ONTOGENETIC PATTERNING OF DEVELOPMENTAL INSTABILITY IN MAMMALS

Hallgrímsson, Benedikt
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Developmental stability refers to the buffering of developmental processes from environmental effects. Ontogenetic patterns of fluctuating asymmetry (FA)—the distribution of random deviations from bilateral symmetry—can be used to distinguish among mechanisms that contribute to variation in developmental stability. Based on large ontogenetic skeletal series of *Macaca mulatta* and *Homo sapiens*, I report that the FA variances of skeletal-metric traits increase throughout postnatal growth. Coupled with the finding that slower growing mammals exhibit higher osteometric FA variances, this result is consistent with the hypotheses that FA in mammalian bone is primarily caused by: a) cumulative effects of asymmetrical mechanical factors, b) a tendency for bone morphology to drift through undirected remodeling during growth, and/or c) accumulation of variation in growth regulation. Limb elements in mouse embryos (12-16 days) are being used to illuminate the relative roles of mechanical and intrinsic regulatory factors in explaining how FA and time are related during onset, differentiation and growth of the skeleton. Serially sectioned left and right embryonic limb buds are being used to determine variation in such intrinsic features as mitotic rate, cell number and size. These parameters are being correlated with a larger morphometric sample of cleared and stained specimens from the same litters.

A-43 ADDUCTOR SPASMODIC DYSPHONIA – AN $H_2{}^{15}O$ POSITRON EMISSION TOMOGRAPHY STUDY

Thomassen, John Michael
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Braun, Allan
National Institute of Deafness and Communicative Disorders, National Institutes of Health

Adductor spasmodic dysphonia (ADS) is a neuromuscular disorder of the arythenoid muscles of the larynx causing their uncontrolled contraction and thereby inhibiting normal speech. This disorder has been successfully treated with botulinum toxin injection into the arytenoid muscles.

Evidence from separate studies suggests that treatment with botulinum toxin has effects on higher levels of the CNS, particularly the basal ganglia. It was the purpose of this project to use positron emission tomography to study the CNS effects of botulinum toxin therapy for patients suffering ADS. The results of this study show that patients with ADS exhibit reduced neuronal activity in the area of the primary motor cortex. Treatment with botulinum toxin showed no significant change in the activity of the primary motor regions of the cortex. However, significantly increased activity occurred in accessory motor areas including Broca's area. The results from this study suggest that ADS is a disorder affecting the primary motor region of the cortex and that its treatment with botulinum toxin injection does not correct the underlying pathology. Instead, this treatment may improve the condition by stimulating the compensatory activity of other motor areas of the cortex.

R C M

ABSTRACTS

Biochemistry and Ophthalmology

A-44 Cloning of an Aspartate Transcarbamylase-Like Sequence from *Toxoplasma Gondii*. IDA A. MEJIAS AND BARBARA H. ZIMMERMANN. Dept. of Biochemistry, Univ. of Puerto Rico, Medical Sci. Campus, San Juan, PR 00936-5067

Toxoplasma Gondii is a single-cell parasite which causes serious and life-threatening infections in immunosuppressed patients and in the fetus. Current treatment is a combination of drugs which interfere with the parasite's production of nucleotides, often causing toxic side effects. A better understanding of nucleotide metabolism in *T. gondii* may help identify enzymes which could be targets for chemotherapy. For this reason we are studying the pyrimidine biosynthetic pathway in this parasite. The presence of the pathway has been established, and some of the enzymes have been partially purified (Asai et al., 1983). We plan to clone, express, and characterize *T. gondii* aspartate transcarbamylase (ATCase), which catalyzes the second reaction in the pathway. A *T. gondii* cDNA lambda ZAP II library was obtained from NIH AIDS Resource and Reagent Program and was converted into a Bluescript library (Stratagene). Degenerate primers were used to amplify an ATCase-like sequence from this library. The PCR products from a nested amplification were ligated into a T-overhang vector (Invitrogen), and sequenced using the Sanger dideoxy method. Clone pIM24 exhibited homology to ATCases. Three residues known to be in the active site of E. coli ATCase are conserved in pIM24. The PCR fragment has higher identity (34-48%) with monofunctional ATCases and lower identity 22-26%) with ATCases domains of multifunctional enzymes. We are using PCR techniques to obtain the full length fragment. (Support provided by RCMI #G12RR03051 and MBRS SOGGM08224).

A-45 Effect of Mother's Education on Nutritional Intake of Their Children in a Puerto Rican Community. I. VARGAS, C. RODRIGUEZ, N. VELEZ, Y. GOMEZ AND A.M. PRESTON. Depts. of Biochemistry and of Pediatrics, Univ. of Puerto Rico, Med. Sci. Campus, San Juan, PR 00936

Knowledge of nutrition can be a factor in determining the types of foods and nutrients selected. Nutrition education is incorporated into the PR school system at all levels so that the greater the number of grades attended, the greater the amount of nutritional information would be available. We have compared 4 groups of women all residing in Cataño, PR and having from 0-6 years of school (Gp 1 n = 55), 7-9 yrs. (Gp 2 n = 109), 10-12 yrs. (Gp 3 n = 333) and more than 12 yrs. of school (Gp 4 n = 167) as to nutritional status of their children. Data was collected from these children, ages 2-11 yrs., when they routinely visited the Cataño Pediatric Center. Normal food intake was determined via use of a semiquantitative food frequency questionnaire and analyzed for nutrient content using Minnesota Nutrition Data System. Comparisons were made to recommended dietary allowances (RDA's) and compliance to the US dietary guidelines (DG's). Results shown a similar RDA's and DG's for children in all 4 groups of mothers with adequate amounts of major and minor nutrients being consumed except for low iron and fiber. Although cholesterol was within suggested limits, sodium and percent fat in the diets were excessive and percent carbohydrate was below the recommended level. We conclude that the number of years of schooling of women residing in Cataño, PR is not a major factor in determining the type and amounts of nutrients in their children's diets. Supported by USDA National Research Institute Competitive Grants Program #94-37206-0602.

A-46 Aqueous Humor Proteins In Human Senile Cataracts. A. CORTÉS VELÁZQUEZ and S. GARCÍA CASTIÑEIRAS. Departments of Ophthalmology and Biochemistry, School of Medicine UPR.

The study included 29 patients undergoing cataract surgery. Slit lamp photographs were taken preoperatorily and used later to classify patients in three groups, using a simple LOCS II scheme (group A: NSII cataracts, n = 13; group B: NSIII cataracts, n = 8; group C: mature cataracts, n = 8). Samples of aqueous humor were taken intraoperatorily from the same patients and were immediately analyzed by electrophoresis in 10% SDS-polyacrylamide gels, together with known MW standards. Protein bands were visualized with a silver staining procedure and quantified by densitometry. Aqueous humor proteins from cataract patients showed a remarkably consistent qualitative pattern with most bands appearing between the 97Kd and 45Kd MW markers, the main fraction being albumin (67Kd, 63%). Transferrin (80Kd) was identified as the quantitatively more important band with MW higher than albumin. When the percent contribution of each protein band to the total area of the densitometric profile was plotted against the severity of cataract, transferrin significatively increased from group A (4.5%) to group C (6.9%), as revealed by variance analysis ($p<0.021$). There was also a correlation between the amount of total protein detected by densitometry and the severity of cataract. We conclude that there is a specific enrichment in transferrin in the aqueous humor as cataractous changes become more extensive, which coexists with a progressive opening of the blood aqueous humor barrier. This could represent either a typical property of the breakdown of the blood-aqueous humor barrier or bear some relationship to the oxidative changes occurring in cataracts.

(Partially supported by NIH RCMI grant # RR03051).

A-47 An *in vitro* model of lens opacification to screen plant extracts and drugs for anticataractogenic activity. J. O. ALEMAN DÍAZ, P. CHAVEZ, A.M. DIAZ and S. GARCÍA CASTIÑEIRAS. Departments of Ophthalmology, Biochemistry, Pharmaceutical Sciences and Microbiology, Schools of Medicine and Pharmacy.

An *in vitro* culture model was developed of hyperglycemic (diabetic) opacification of the lens (cataract) in which freshly, aseptically excised dog lenses were exposed to 50 mM glucose in an RPMI 1640 complete incubation medium at 37°C under a CO_2 atmosphere. Mild lens opacification, relative to controls, was already evident after 3-4 days and continued to increase with time. Changes in lens optical density and size (perimeter) were captured with a Dage video camera and were analyzed with the Micro Computer Imaging Device Image Analysis Program MCID-M2, upon calibration with known density or length standards. Ethanolic extracts were prepared from plants which have been used in folk medicine for ophthalmologic purposes: *Citrus Aurantum* (CIT) *Tecoma Stens* (TS) and *Centella Asiatica* (CEN). Extracts were evaporated to dryness and the powder was dissolved in the culture medium at a final concentration of 100 μgr/ml. This concentration gave mild toxicity in the Brine Shrimp assays. Images taken for up to 10 days showed that the CIT extract was quite effective in inhibiting the hyperglycemic opacification of the lens, while the TS and CEN extracts promoted opacification. The TS extract induced in addition a yellow pigmentation of the lens. The *in vitro* model described here is therefore useful for the screening of potential anticataractogenic drugs. Experiments are in progress to further characterize the substance(s) present in the CIT extract responsible for its ability to relieve the hyperglycemic stress on the lens.

(Partially supported by NIH grants #RR03051 (RCMI) and #RR10852).

A-48 The Reaction of Albumin with Glutaraldehyde and its Relevance to Lens Aging and Cataractogenesis. A. OLIVER, S. BENITEZ and S. GARCÍA CASTIÑEIRAS. Departments of Ophthalmology and Biochemistry, School of Medicine, UPR.

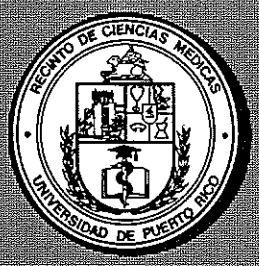
The spontaneous formation of Schiff bases *(non-enzymatic browning)* is responsible for the glycosylation of proteins in diabetes and may contribute to lens degenerative changes associated with aging and cataracts. The *in vitro* reaction of glutaraldehyde (GA) with albumin (BSA) was followed as a model of Schiff base formation. BSA (1 mg/ml) and 1% GA were allowed to react for several weeks at room temperature in the dark, in a 0.1 M phosphate buffer pH 7.0 and in the presence of 0.1% SDS and 0.01% azide. The reaction mixture was periodically scanned for UV-visible absorption and for tryptophan (T) and non-tryptophan (NT) fluorescence. Controls were included without GA or albumin. T-fluorescence did not vary with time. NT-fluorescence started to increase immediately to level off after 20 days. EX/EM maxima centered at about 325/405 nm with smaller peaks at 345/440 nm. Absorption increased in the UV region (350 nm) without invading the visible region. The appearance of NT-fluorescence and the increase in 350 nm absorption not derived from the degradation of T thus represent a convenient way to follow Schiff base formation. Changes were compared to those resulting upon exposure of proteins to UV light and to those described in the human lens during aging and senile cataract formation. The BSA/GA reaction may be used as an *in vitro* model of some of the changes taking place in the aged/cataractous human lens and to test the effect of drugs on the underlying chemical mechanisms.

(Partially supported by NIH RCMI grant # RR03051).

A-49 Prevalence and Factors Associated with Severity of Retinopathy in Hispanic Diabetics in Dialysis at the Puerto Rico Medical Center San Juan, Puerto Rico. Norma L. Zapata, M.D., Dept. Ophthalmology, Carlos Rivera Bermúdez, M.D., Dept. Internal Med., UPR-Sch. Med., Med. Sciences Campus, San Juan, P.R.

The objective of this study is to measure the prevalence of diabetic retinopathy and visual loss in the dialysis population at the University Hospital Renal Center. Diabetics account for approximately 30% - 40% of all dialysis patients; therefore, their quality of life and treatment outcomes have to be assessed. To the best of our knowledge, in Puerto Rico this has not been studied. We propose a pilot study of the diabetics at the Renal Center. It will consist of a cross-sectional, descriptive investigation during April of 1997 to determine how many patients have retinopathy and visual loss. A description of which factors may be associated with the condition is also included in the evaluation. Diabetic patients will be recruited using the following criteria: diabetic (IDDM or NIDDM) and receiving dialysis treatment at the University Renal Center. The medical records of those recruited will be reviewed and patient interviews will be conducted using a questionnaire to obtain the necessary data. The prevalence of retinopathy and blindness will be determined using a complete ophthalmologic evaluation and fundus photographic grading technique. We expect to find diabetic retinopathy present in the dialysis population at the University Renal Center.

Partially supported by HCOE Grant.



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ABSTRACTS

School of Dentistry and Public Health

A-50 ***Assessment of a Community's Oral Health Status.***

A. ELIAS*, R. BAEZ, K.CRESPO, J.GIUSTI,C.TORO, M.BAEZ, R. WOOD (UPR,School of Dentistry, San Juan, Puerto Rico and UTHSC, San Antonio, Texas).

An overall oral health assessment in Puerto Rico has not been conducted in the last four decades. The Commonwealth of Puerto Rico, including the municipality of Culebra, has no community fluoridation program at present. The objectives of this study were to determine the oral health status of the population in the island municipality of Culebra, Puerto Rico; to conduct a pilot study in order to determine the feasibility of using World Health Organization (WHO) criteria and methodology for oral epidemiological surveys in Puerto Rico; and to explore the need of developing community preventive programs. Judgment samples for the following age groups were obtained: 12 (n=23), 19-25 (n=16), 35-44 (n=45), 65 and over (n=32). Total number of participants evaluated was 154, 10% of the Culebra population (1990 Census). Examinations were performed following a calibration exercise, using WHO guidelines. Percent agreement and Kappa statistics were calculated. The following indicators were used: DMFT, CPI-Loss of Attachment, Opacities/Hypoplasia, TMJ Assessment, Oral Mucosa, Dental Fluorosis, Prosthetic Status and Need, Dentofacial Anomalies, and Need for Inmediate Care. Among the most important results obtained were a DMFT of 4.3 (SE 0.9) for 12 year olds, considered moderately high according to WHO criteria. The caries prevalence for this age group is apparently higher than the DMFT of 2.8 (SE 0.2) for 12-17 years reported for USA 1988-91. Furthermore, only 30% of this age group was caries free. The DMFT for 19-25 years old was 9.63 (SE 1.5), 13.47 (SE 2.0) for the 35 to 44 age group and 23 (SE 5.6) for the 65 and older age group. A fluoride concentration in drinking water of less than 0.12 ppm was found. In the 19-25 age group gingival bleeding was observed in an average of 2.1 sextants. For the 35-44 age group, the mean number of sextants with pockets of 4 mm+was 2.1. Thirty seven and a half percent of the 65+ group were edentulous. WHO criteria were useful to obtain an overall assessment of this community; however, future research should consider other frequently used dental measurements for comparisons with USA population groups. The levels of disease dictate a need for primary preventive programs such as systemic fluorides and education. Also, intervention programs in restorative dentistry and periodontics are needed to reduce disease prevalence.

A-51 ***Análisis Comparativo de la Tasa de Utilización de Servicios de Salud Oral en la Población de Cero a Trece años en Puerto Rico. *J. Giusti, K. Crespo, I. Alvarez, I. Lorenzi, Y. Rojas. Escuela de Odontología, Recinto de Ciencias Médicas, UPR, San Juan, PR.***

Existen controversias en cuanto a la edad en que un niño(a) debe realizar su primera visita al dentista. No obstante, los distintos profesionales de la salud reconocen la necesidad de una evaluación buco-dental antes de los tres años de edad. El examen de los datos de la Muestra Contínua de Salud del Departamento de Salud de Puerto Rico en el año 1989 indicó que la proporción de niños menores de 6 años que nunca ha visitado al dentista era de 86 porciento.El propósito de esta investigación fue determinar los niveles de utilización de servicios de salud oral en niños(as) de 0 a 3, 4 a 5 y 6 a 13 años en Puerto Rico durante los años 1993-94 y 1994-95. Se recopilaron y analizaron datos sobre la utilización de servicios dentales en una muestra aleatoria de 108 oficinas de dentistas generalistas y 20 odontólogos pediátricos. Se obtuvo una muestra aleatoria de 50 expedientes en cada oficina para un total de 5,400 expedientes en oficinas de generalistas y 840 en oficinas de dentistas pediátricos.Del total de niños de 0 a 13 años en las oficinas de odontopediatras, el 4.1% correspondía al grupo de 0 a 3 años, el 12.9% al de 4 a 5 años y el 83% al de 6 a 13 años. En las oficinas de generalistas el 1.4% correspondía al grupo de 0 a 3 años, el 4.5% al de 4 a 5 años y el 94% al de 6 de 13 años. En las oficinas de odontopediatras el promedio de visitas anuales era de 2 para el grupo de 0 a 5 años y 3 para el de 6 a 13. En las oficinas de generalistas el promedio de visitas anuales era de 3 para ambos grupos de edad.A partir de los datos de las oficinas de generalistas se estima que la tasa de visitas al dentista generalista en Puerto Rico es de 0.02 para el grupo de 0 a 3 años, de 0.12 para el de 4 a 5 y 0.51 para el de 6 a 13 años, esto en comparación con una tasa de 1.0 para el total de la población. Del tipo de servicio ofrecido es interesante notar que sólo el 8% de los niños (as) en las oficinas de los odontopediatras recibieron servicios de sellantes de fosas y fisuras.De los hallazgos de este estudio sobresale la baja utilización de servicios dentales para los niños (as) de 0 a 13 años, particularmente en los menores de 3 años para los cuales la utilización es casi ninguna.Es necesario desarrollar programas de educación a la comunidad y a los profesionales de la salud sobre la importancia de una visita temprana al dentista y de los sellantes de fosas y fisuras.

A-52 Occupational Dermatitis among Migrant Farmworkers at Dover, Delaware

By R. Torres, R. Rullan, C. Sylvestre and L. Burgos
George Washington Univ. Medical Center
Div. of Occup. and Envio. Med. Wash., D.C.

An interviewer administered questionnaire was conducted in farmworker camps in Dover, Del. during June and July 1996 to determine self-reported prevalence of rash among migrant farmworkers. All the workers in the eight camps identified by the outreach workers of Delmarva Rural Ministries were approached for interview resulting in a 91% participation rate. Data was entered into and analyzed using EpiInfo. Seventy six percent of the population was male with an average age of 30. Eighty two percent of the participants reported being from Latin America and the remaining 18% from the continental US. Out of the final sample of 121 farmworkers, 22 reported having rash while in the current job. Self-reported skin exposures to pesticides was associated with self-reported rash (x^2=5.27, p=0.02). This data suggests that exposure of skin to pesticides seems to be a risk factor for dermatitis in this population. In addition, thirty percent of the farmworkers reported having received pesticide training. A significant relationship was also found with having been trained on how to handle pesticides and the use of personal protective equipment (PPE), specifically long sleeved shirts (p=0.04) and gloves (p=0.02). Thus data suggests training influences self protective behavior. Furthermore data suggests that most of the migrant farmworkers in this study are working in sites that are not in complete compliance with Osha field sanitation standards. This study was funded by the NIEHS by way of the Div. of Occup. and Envio. Medicine at the GWUMC.

A-53 Epidemiologic Profile of AIDS Cases in Puerto Rico: 1981-1996

R. Pérez, MD, MPH, PhD, E. Suárez, MSc, PhD, C. Pérez, MS, PhD, A. Morales, MD, MPH. Graduate School of Public Health.

Objective: To describe the epidemiologic profile of the population affected by HIV/AIDS in Puerto Rico.
Methods: Analysis and interpretation of epidemiologic data of the Puerto Rico AIDS Surveillance System.
Results: From January 1, 1981 through September 30, 1996, 18,711 cases have been reported in Puerto Rico. Males were disproportionately affected with AIDS, with an overall male-to-female ratio of 3.6. Adults comprised the majority of the cases (97.6%), and the age group most affected was 30 to 34 years. The region of San Juan accounted for 62% of these cases. The predominant mode of exposure reported was intravenous drug use (IDU), accounting for 51.5.% of all reported cases. Among females the predominant mode of exposure was heterosexual contact, accounting for 54.5%. Among males who reported heterosexual contact, the most affected age-group was 50 or more. Among females, the largest percentage occurred in the 30-39 age group. Data from recent years suggest that the male-to-female ratio has been changing reflecting the expansion of the AIDS epidemic among women. The median survival time of AIDS cases in Puerto Rico after diagnosis was 15.4 months for males and 22.8 for females ($p<0.5$).
Conclusions: Puerto Rico is one of the most affected areas in the US and its territories. Interestingly, the leading mode of exposure (IDU) was different to the leading mode in US. Heterosexual contact is increasing, primarily, in young females. However, males are affected later in life. This epidemiologic profile underscores the disproportionate impact of the AIDS epidemic in Puerto Rico and the need for imperative preventive measures directed to target groups, especially drug users and young heterosexual women. Funded by a Ryan White contract.

A-54 Description of Childhood Cancer in Puerto Rico, 1980-1991

R. Pérez MD, MPH, PhD, Rodríguez Linnette, MS. Graduate School of Public Health.

Objective: To describe the proportion of pediatric (<20 years) cancer cases in Puerto Rico from 1980 through 1991.
Methods: Analysis and interpretation of all new childhood cancer cases reported to the Puerto Rico Cancer Registry between the years 1980 through 1991, who resided in Puerto Rico, and for whom a histologic type was provided.
Results: From 1980 through 1991, a total of 1,814 new pediatric cancer cases were reported, of which 52.2% were aged <10 years, 18.7% were between 10 to 14 and 29.1% were 15 to 19. Most of the cases resided in urban areas (58.5%), and the largest number of cases was reported in San Juan (12.5%). Leukemia was the most common diagnosis in children of all ages (31.2%), followed by lymphomas and other reticulo-endothelial neoplasms (16.3%), and brain central nervous system tumors (15.8%). No renal tumors were reported. The most frequent subtype of leukemias was lymphoid leukemia accounting for 72% of all leukemias. The most common form of lymphomas was Hodgkin's disease (8.8%). Among brain tumors gliomas accounted for 15.0%. The most common site of cancer tumors were brain (17.2%), blood amd lymph tissues (16.5%), and bones and joints (6.3%). Some differences in the distribution of the cancer cases by gender, age, and residence area were observed.
Conclusions: Cancer is an important cause of morbidity in children and adolescents in Puerto Rico. Overall, these findings are consistent with previous studies in the U.S. However, there were some important differences in the distribution of histologic types when these results were compared with similar studies in countries such as France and with the results of the National Cancer Institute's Surveillance, Epidemiology and End Results (SEER) Program. These differences could provide clues regarding the etiology of the disease. Funded by CIDIC

A-55 Land Use Patterns and Fecal Contamination of Coastal Waters of Western Puerto Rico

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This study, funded by NASA, found there is a significant relationship between watershed land cover and microbiological water quality of rivers flowing into Mayagüez Bay in Western Puerto Rico. Land covers in the Guanajibo, Añasco, and Yagüez watersheds were classified into forested areas, pastures, agricultural zones and urban areas so as to determine relative contributions to fecal water contamination. The land cover classification was made using Landsat images and the reflection patterns on infra-red, green and blue bands in aerial photographs. Significantly larger average pathogen indicator densities appear in the Yagüez River (508 PFU/100mL of coliphages), which drains the watershed with the highest urban density of the three (5.18% high density urban). The Añasco River showed the lowest coliphage density near its mouth (63 PFU/100mL), and drains a mostly agricultural watershed (0.99% urban). The Guanajibo River watershed drains a mixed land cover area (7.41% low density urban) and shows an intermediate coliphage average density near its mouth (67 PFU/100mL). While urban density correlates with pathogen indicator density, no significant statistical correlation was found between stream flow and density of the different microbiological water quality indicators used. This is probably due to raw wastewater discharges coming from sanitary sewer bypasses into study streams during frequent pumping station failures. The direct effect of nonpoint source contamination on streamwater quality cannot be observed under these circumstances.

A-56 La mujer frente al aborto,

AL DAVILA, Ph.D., A COLON, Ph.D., MD FERNOS, JD, E VICENTE, JD, EGSP, RCM, UPR

Ante las amenazas experimentadas en Puerto Rico de restringir el derecho al aborto, el presente estudio explora la trayectoria sociopolítica del debate y los discursos a través de los que se ha desarrollado la discusión de los sectores pro-opción y antiaborto en una situación de legalidad como la que prevalece en el derecho puertorriqueño. En este estudio se examinan las condiciones que imponen los intentos de deslegitimación del aborto sobre las mujeres y los diferentes sectores de la comunidad; se toman en consideración tres niveles de análisis:

- los supuestos filosófico, teóricos y jurídicos que enmarcan las propuestas de restricción vis a vis las que proponen mantener el estado de legalidad del aborto
- el estudio sociopolítico de los sectores que promueven estas líneas de argumentación y los intereses que la propulsan
- la exploración de los códigos ideológicos entre las mujeres en torno a su sexualidad, su cuerpo, la maternidad y el feto.

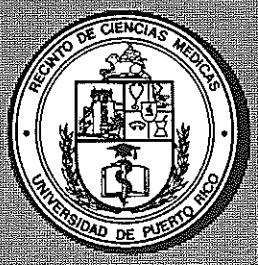
Se ha utilizado la metodología de análisis de contenido para el estudio de los discursos de sectores organizados y grupos focales de mujeres para investigar el resultado de estos debates.

Se desprende del análisis realizado que los intentos de establecer restricciones al aborto en Puerto Rico se ejemplifican en las vistas legislativas examinadas tanto en el ámbito civil como el estatal. La lucha desatada ante estas medidas por los sectores que defienden los derechos de las mujeres han impedido por el momento la aprobación de los intentos de deslegitimación. También se señala que se ha solidificado el derecho exclusivo de las mujeres a la opción de decidir sobre sus cuerpos.

A-57 The Effect of a Full and a Keyword Spanish Questionnaire Translation on Hispanics' Mail Survey Response Rate

WANDA I. ALTRECHE BERNAL, Ph.D.
School of Nursing, Medical Science Campus

The purpose of this study was to examine the effect of a full and keyword Spanish questionnaire translation on Hispanics' mail survey response rate and response quality. A secondary purpose was to analyze the cost-effectiveness of both kinds of translations. The experimental design consisted of three comparison groups of Hispanics and one group of Anglos. All the groups were equal in size (230) for a total random sample of 920. The subjects were parents who had a child enrolled in the participating schools of one Florida School District. A questionnaire in English, Spanish, or keyword translated to measure satisfaction with the school and the school district among parents was administered to the different groups included in the sample. A total of 164 (19%) responses were used to report the data of this study. Descriptive statistics, chi-square, Kruskal-Wallis, and Wilcoxon statistical tests, and cost-effective analysis were computed. The hypothesis tests revealed no significant differences in response rate among the groups. Quality was examined in terms of item omission and inadequate responses. Significant differences in quality were found among the groups. The Spanish translation of the questionnaire had the highest number of respondents who omitted more than one item (57%), followed by the keyword translation (42%). Also, the Spanish and keyword translations had the highest number of respondents who provided inadequate responses (45% each). The cost-effectiveness analysis revealed that none of the translations were cost-effective. Both had higher costs than the English version and did not increase the response rate.



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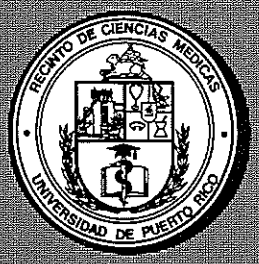
ABSTRACTS

Poster Presentations

April 16-18, 1997



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ABSTRACTS

Clinical and Basic Sciences

A-58 Helminthiases of *Rattus* spp. in Northern, Southern and Central Puerto Rico and Cayo Santiago. Christina MALDONADO and W. J. KOZEK. Department of Environmental Health, School of Public Health, &Department of Microbiology & Medical Zoology, Medical Sciences Campus, University of Puerto Rico.

Previous study to define the profile of helminthic fauna of Puerto Rican murines, and to identify the zoonotic species, was continued by trapping and examining rats captured in Adjuntas, Cayo Santiago, Maricao, Pañuelas, Trujillo Alto and Ponce. The 62 rats ((22 *Rattus rattus* and 40 *R. norvegicus*) examined harbored a total of 15 species of helminths: *Strongyloides venezuelensis, S. ratti, Nippostrongylus braziliensis*, strobilocercus of *Taenia taeniaformis, Capillaria hepatica, Angiostrongylus cantonensis, Trichosomoides craussicauda, Ganguleterakis spumosa, Ecoleus gastricus, Gongylonema neoplasticum, Mastophorus* sp., *Hymenolepis diminuta, Moniliformis moniliformis*, and and unidentified trichostrongylid and a trematode. Four of the recovered helminths: *C. hepatica, A. cantonensis, H. diminuta* and *M. moniliformis* can infect man. Some of the helminth species appear to have a broad distribution throughout the Island; distribution of others, e.g. *E. gastricus. G. spumosa* and the unidentified helminths appear to be more limited. These results confirm our previous observations of high prevalence of helminthiases in local rats, and the presence of zoonotic species which are of potential hazards to human health. This study will be continued to characterize more completely the helminthic fauna of local *Rattus* spp. by examination of murines from other areas of Puerto Rico from the neighboring islands.

A-59 **Conocimientos y creencias sobre cáncer de mama y prácticas de detección temprana en mujeres puertorriqueñas de edad avanzada** M. OLIVER-VAZQUEZ, M. SANCHEZ-AYENDEZ, E. SUÁREZ PEREZ, H. VELEZ-ALMODOVAR. Escuela Graduada de Salud Pública, U.P.R.

El propósito de este estudio es identificar las barreras personales y externas que influyen en la decisión de las mujeres puertorriqueñas de 65 años o mayores, para cumplir con las prácticas de detección temprana de cáncer de mama. Se utilizó la metodología cualitativa de grupos focales para investigar los conocimientos y las creencias sobre el cáncer de mama de 62 mujeres de edad avanzada. Se organizaron 10 grupos de discusión de acuerdo a la zona de residencia y al nivel educativo de las participantes. Los temas discutidos fueron: conocimientos y creencias sobre el cáncer de mama, información provista por los profesionales de la salud, exámenes de cernimiento ordenados por su médico y razones para no llevar a cabo las prácticas de detección temprana. Mediante un análisis de contenido se identificaron las áreas de preocupación de las participantes con relación al tema, los asuntos principales discutidos en los grupos y el vocabulario común utilizado. Las razones para no llevar a cabo prácticas de detección temprana fueron entre otras: falta de conocimiento, no sentirse susceptible a adquirir la enfermedad, pudor o molestia, temor a encontrarse un nódulo, falta de orientación de parte de los profesionales de la salud, confianza en que su médico hará los exámenes correctamente, alto costo de los exámenes de cernimiento y falta de transportación. El análisis refleja un mayor conocimiento sobre el cáncer de mama y un mayor cumplimiento de las prácticas de detección temprana en las mujeres profesionales al compararlas con las no profesionales. El temor y el pudor fueron las razones principales para no hacerse el autoexamen del seno, tanto en las mujeres profesionales como en las no profesionales. Los resultados obtenidos en esta primera fase de la investigación fueron utilizados para la construcción de un cuestionario culturalmente apropiado para las mujeres de 65 años o más, residentes en Puerto Rico.

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A-60 **Análisis de Sobrevivencia de Pacientes Dializados en Puerto Rico, 1970-1994**
E. Súarez, MSc, PhD, R. Pérez, MD, MPH, PhD, R. Burgos, MD, C. Morell, MSc, Departamento de Bioestadística y Epidemiología, Escuela Graduada de Salud Pública, Consejo Renal, Puerto Rico.

Objetivo: Evaluar las probabilidades de sobrevivencia en pacientes con Enfermedad Renal Permanente (ERP) en Puerto Rico, 1970-1994.
Métodos: Se utilizó el método de Kaplan Meier para determinar la tasa de sobrevivencia de diabéticos y otros diagnósticos por sexo, grupos de edad, modalidad de tratamiento y regiones de salud.
Resultados: El análisis incluyó 7,527 pacientes reportados al sistema, de los cuales, 4,295 (57%) se reportaron como fallecidos al final del tiempo de estudio, 3,235 se clasificaron como censurados. El tiempo mediano de sobrevivencia (TMS) para todos los pacientes fue de 47.7 meses (95% IC: 45. 70, 50.0). Se encontró una sobrevivencia significativamente menor (p=0.0001) para los diabéticos comparados con todos los otros diagnósticos; el TMS para los diabéticos fue de 29.2 meses (95% IC 27.7,31.4). Al estratificar los diabéticos por sexo, se encontró que en el tiempo mediano de sobrevivencia menor para las mujeres (p=0.0001). La edad fue un fuerte predictor de la sobrevivencia (p=0.0001) con el TMS menor en el grupo de edad > de 59 años, 26.6 meses (95% IC: 24.5,28.3). En general, la modalidad de tratamiento con la sobrevivencia menor fue hemodiálisis con 59.4 meses (95% IC: 56.5, 63.1), (p=0.0001).
No se encontró asociación significativa en la probabilidad de sobrevivencia por sexo ni por región de salud (P>0.05). Concluimos que en la población de Puerto Rico, la diabetes, las personas de edad avanzada y la modalidad de hemodiálisis tienen menor probabilidad de sobrevivencia. Se necesitan análisis adicionales para poder explicar estos hallazgos. Financiado por el Consejo Renal de Puerto Rico.

A-61 Epidemiology of AIDS in the San Juan Standard Metropolitan Statistical Area. C.M. Pérez, PhD; R. Pérez-Perdomo, MD, MPH, PhD; E. Suárez, PhD; Department of Biostatistics and Epidemiology, Graduate School of Public Health, UPR, MSC.

To describe the epidemiology of AIDS in the San Juan Standard Statistical Metropolitan Area (SMSA), information on all AIDS cases reported to the

Puerto Rico AIDS Surveillance System from January 1981 through September 1996 was analyzed. As of September 30, 1996, 11,597 cases have been reported, accounting for 62% of all cases reported in Puerto Rico. This represents an increment of 15% from the 10,090 cases reported in September 1995. In addition, the number of AIDS cases reported during 1995 (1,292) was lower than the numbers reported during 1994 (1,677) and 1993 (2,025), reflecting the waning effect of the expanded 1993 AIDS surveillance case definition. Of the 11,597 cases reported, 7,586 have died, giving an overall case fatality ratio of 65%. Males were disproportionately affected with AIDS, with a male-to-female ratio of 3.7. However, in 1995, females accounted for 24% of cases, the highest proportion yet reported. Adults (≥20) comprised the majority of the cases (98%), and overall, the 30-39 age group was the most affected (45%). Intravenous drug use (IVDU) was the predominant mode of exposure (51%) followed by heterosexual contact (20%) and homosexual contact (18%). Among males, the predominant modes of exposure were IVDU (54%) and homosexual contact (23%). Among females, the predominant modes of exposure were heterosexual contact (52%) and IVDU (39%). Comparison of risk behavior over the last two years demonstrate a shift from the predominantly IVDU spread toward the pattern of heterosexual transmission. The proportion of cases who reported IVDU has decreased (13%), while that among heterosexual (20%) and homosexual (11%) contact have increased. In the San Juan SMSA, the estimated number of HIV infected people alive in September 1996 was nearly 20,616, of which, 78% were males and 22% were females. The median survival time after diagnosis was 14.3 months (95% CI: 13.5, 15.1) for males and 20 months (95% CI: 17.8, 22.4) for females. This analysis accentuates the need of specific actions within high risk groups to curb the further spread of HIV/AIDS. Health professionals should play a more aggressive role in counseling people about preventive measures to reduce their risks. This research was supported by a grant from Ryan White Funds.

A-62 **A Qualitative Analysis of Service Needs and Barriers among HIV/AIDS Patients in Puerto Rico.**

M. SANCHEZ-AYENDEZ, R. PEREZ-PERDOMO, H. VELEZ-ALMODOVAR. Graduate School of Public Health, U.P.R.

The objective of this study was to conduct a qualitative service needs and barriers assessment of patients diagnosed with HIV/AIDS. Focus groups were used to explore a range of concerns pertaining to the needs and barriers that different sub-populations confront in terms of services. The selected populations were: ex-IDU, homosexuals, lesbians, and heterosexual women receiving care in the public health delivery system. A session with patients receiving private medical care was also held. Seventy-three persons participated in ten focus-group sessions. Group size varied from four to eleven participants. The age range was from 21 to 53. Needs were divided into medical and social support. Barriers were identified along the same lines. Results were analyzed according to: similarities and differences among the various high-risk groups. In terms of medical needs, all the groups from the public health system expressed a desire for a better organization and coordination of services as well as for a wider availability of medicines, particularly protease inhibitors. More access to specialists was also stressed. Transportation and formation of peer-support groups were important social-support issues for all sub-groups. In terms of barriers to medical services, all the groups highlighted the existing system of appointments and lengthy waiting period at public health services. Discrimination and insensitivity from some service providers was also pinpointed as well as the high cost of retroviral drugs. Most groups mentioned inadequate transportation and lack of information about existing services as barriers pertaining to social support. Particular needs and barriers by high-risk group were also analyzed. The heterosexual women were the only participants who stressed that their familial and domestic responsibilities presented conflicts in terms of attending medical appointments. They also emphasized the formation of peer-support groups for family members as a social support need. The different sub-groups also commented on the need for differentiating among subgroups of HIV/AIDS patients in terms of provision of some services.

Funded by a "Ryan White " contract.

A-63 **INFLAMMATORY BOWEL DISEASE: Demographic characteristics of puertorrican patients. A progress report.**

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BACKGROUND: Crohn's disease (CD) and Ulcerative Colitis (UC) are inflammatory bowel diseases that primarily affect young patients. Women and patients from higher socioeconomical status, living at urban areas tend to be more commonly affected. Smoking correlates positively with CD and negatively with UC. **PURPOSE:** To evaluate the demographic characteristics of puertorrican patients with IBD, compare them with IBD mainland patients and establish a Registry of IBD patients in Puerto Rico. **METHOD:** The patients have been enrolled in the study since 1995. A questionnaire of demographic characteristics and clinical data was designed. The patients were interviewed either personally or by phone. It was approved by the Institution Review Board of the MSC and informed consent was obtained. **RESULTS:** 60.7% of our population are female with a mean age of 37 years, 34.5% live at the metropolitan area, 59% are from urban areas, 74% have a high educational level, 60.1% are married, 84% are of low socioeconomical status, 72% are non smokers and 7.5% have family history of the disease. **CONCLUSION:** The majority of our demographic characteristics are similar to literature. However, our study showed that the majority of our population is married, of high educational level although from low socioeconomical status.

A-64 **An assistive technology interdisciplinary service model**

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The biomedical sciences are traditional contributors to the quality of life of humankind. Technology is instrumental in the prevention of health conditions and in the preservation of life and quality of life. As technology becomes a state of the art in the medical professions, other professionals, such as engineers and rehabilitation professionals, are becoming involved in the problem-solution processes in health. Service model alternatives based on individual needs is the outcome that follows, where interdisciplinary intervention is the baseline to attain the health goals of preservation and improvement of life and it's quality, specially for persons with disabilities. The Puerto Rico Assistive Technology Project, College of Health Related Professions, Medical Sciences Campus of the University of Puerto Rico, in collaboration with the Mayagüez School of Engineerings, has created a model for the development of assistive technology according to the particular needs of persons with disabilities. This model is an example of an excellent cost-effective endeavor combining biomedical and technology-related best practices. Details will be presented.

A-65 Reliability of skeletal specimens for inferring angular movements in primate postcrania: Comparison of angular values that define the potential ranges and limits of forelimb movements in living and skeletonized rhesus macaques. G.M. HERNANDEZ, College of Allied Health Professions, J.E. TURNQUIST, J.G.H. CANT, and M.A. SCHOEN, Department of Anatomy, University of Puerto Rico, San Juan, PR.

To infer the functional morphology of fossil forms requires analysis of living taxa. It is a common practice to estimate locomotor and positional behavior using skeletal material housed in museums, rather than measurements of living individuals. In this study the reliability of estimating ranges of movement in live animals from skeletal specimens was evaluated by comparing flexion and extension at the elbow joint and pronation and supination of the forearm. The potential range of these motions was measured using the left humerii, ulnae, and radii of 30 adult skeletonized *Macaca mulatta* (15 female and 15 male) at Caribbean Primate Research Center. Comparable measurements were made by manipulating the forelimbs of a similar sample of chemically restrained animals. Bones were positioned according to either published descriptions or anatomical features derived from examination of radiographs of living animals and bones. Comparison of measurements taken from living and skeletal specimens indicates that the limits of elbow flexion and extension can be estimated reliably from bones. Estimates of limits of forearm pronation and supination from bones however were less than those from live animals. Further investigation on estimating these forelimb movements from skeletal material is warranted by the importance of limb bone rotations in primate behavior. This research was supported by the School of Medicine of the University of Puerto Rico.

A-66 BONE DENSITOMETRY AMONG AN ALBINO POPULATION IN P.R. J.A. Montalvo Figueroa, MD; F. Aquiló Jr., MD, FACP, FACE; Cynthia Rodríquez, BDT; Vanessa Alicea, MD; University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

During the past 2 decades the problem of osteoporosis has gained interest, and many metabolic and densitometry studies have been done. Factors such as sex, age, sun exposure, medications and skin color have gained relevance on the topic. It has been estabilished that dark skin people have increased bone mineral densities (BMD) when compared to light skin cohorts. To our knowledge there hve been no reports in the literature of BMD among the albino population, who represent the lightest skin coloration. Therefore, we have studied 13 albino patients (8 females, 5 males) and have compared them with age and sex matched controls (13 female, 5 males) with similar Body Mass Indexes (kg/m^2)(BMI) as a pilot study in Puerto Rico. The present study reports findings on the above population. We performed both single photon (SPA) and dual energy (DEXA) absorptiometries. Results showed a significant decreased BMD among albino subjects vs. control. Females albinos had hip BD of 0.811 gm/cm^2 vs. 0.911 gm/cm^2 ($p < 0.02$), lumbar spine 0.952 gm/cm^2 vs. 1.073 gm/cm^2 ($p < 0.05$). In men, respective values were 0.902 gm/cm^2 vs. 1.015 gm/cm^2 ($p < 0.02$) and 0.879 gm/cm^2 vs. 1.144 gm/cm^2 ($p < 0.03$). On SPA no significant differences have been found so far. This preliminary study on a small population suggests that the albino population has lower BMD. This could put them at increased risk for osteoporosis and fractures during their life. The study is being expanded and posible mechanisms searched for.

A-67 **Comparison of Fluorescent Calibration Standards Used in Quantitative Flow Cytometry Immunophenotyping Analysis as a Funtion of pH Environment.** M. Méndez, G. Santiago, L. Díaz, A. Schwartz and E. Fernández-Repollet. Dept of Pharmacology, UPR School of Medicine, San Juan, PR.

One of the primary uses of fluorescent calibration standards in flow cytometry is to quantitate the fluorescence intensity or antibody binding capacity of cells labeled with fluorescent antibodies. Four commercial calibration standards Quantum 26-FITC (FCSC, San Juan PR), Rainbow Calibration Particles (SpheroTech, Libertyville IL) and Linearflow Green (Molecular Probes, Eugene, OR) were evaluated. A sample of lysed whole blood and Quantum Simply Cellular calibration standards (FCSC,San Juan, PR) labeled with CD3-FITC (BDIS, San Jose, CA) were equilibrated in a series of ISOTON II buffers, which pH was adjusted across a range from 6.0 - 9.5. All standards and cell samples were then run on a FACSort flow cytometer (BDIS, San Jose, CA) at the same instrument settings (e.g., FL1 PMT 653). The cell samples, Quantum Simply Cellular and Quantum 26 FITC calibration standards exhibited a sigmoidal increase in fluorescence intensity while the Rainbow Calibration and the Linear Green standards show no increase in intensity across the experimental pH range. These data demonstrate that accurate quantitative fluorescent measurements require that the standards used respond to the changes in pH environment in a manner similar to the cells to be analyzed. Supported by Grant No. 2 S06 GM08224.

A-68 **Isolation of Colorectal Cancer Genes from Puerto Rican Patients by Means of Differential Display**
M. Jordan, R. López, A. Cardona, C. Neri, B. Jiménez. Departments of Pharmacology and Surgery, School of Medicine, and School of Pharmacy, MSC; Oncological Hospital.

Colorectal cancer (CRC) is an inherited disease that arises from a multistage process involving the activation of proto-oncogenes and/or inactivation of tumor suppressor genes. Although some of these affected genes have been identified and associated with the development of this pathological condition, a complete understanding of the mechanisms and biochemical processes involved is yet to be obtained. Very little research in this field has been performed employing the latest methodology of Differential Display (DD). DD is a novel approach in molecular biology that has several technical advantages over other existing methods. Briefly, the method involves the reverse transcription of mRNAs with an oligo-dT anchored primer followed by a PCR in presence of a second arbitrary primer. The amplified cDNA fragments are labeled with ^{35}S and

displayed on a DNA sequencing gel allowing direct comparison side-by-side with the control and experimental subsets. The differentially expressed cDNA fragments are then isolated, cloned and sequenced for further characterization of these genes. We have assayed two different sets of normal and cancerous tissues from two patients subjected to colectomy. The results from the differentially displayed gels obtained from the tissues showed a total of nine bands, six represent inhibited genes and three represents induced genes. Two of these bands were analyzed for true positive identification. One of the isolated fragment representing an induced gene was confirmed as a being a true positive using Northern Blot, while the other analyzed fragment representing an inhibited gene did not yield any positive confirmation. The fragment identified as a true positive was reamplified by PCR and partially sequenced (150bp). The PCR product was used as a probe in a Norhern Blot to identify its complementary mRNA sequence which yield a molecular weight of about 4,000 nucleotides. The partial sequence was used to compare with known sequences of the Genbank data base (NIH). No homology was found with any known gene. These data suggest that this isolated fragment may be a novel sequence of an induced gene during the multistage process of CRC. In order to confirm this the complete sequence of the isolated cDNA fragment needs to be obtained. We have cloned this cDNA fragment with pCR2.1 vector and INVαF' competent cells from a TA Cloning Kit to determine the complete sequence.

A-69 **Analysis of Adhesive Force and Drug Diffusion From Glipizide Hydrogel Systems.** **J. GARCIA* AND E.S. GHALY: School of Pharmacy, Medical Sciences Campus, University of Puerto Rico.**

Many controlled release therapeutic compounds are administered orally. However the gastro intestinal short transit time and motility represent a serious problem facing the controlled release systems. In this study different bioadhesive glipizide systems containing Carrageenan as a mucoadhesive polymer were developed and evaluated. The objective of this study is to measure the work of adhesion required to separate the different bioadhesive formulations from rabbit tissues. Also to evaluate the diffusion coefficient of the drug from these systems. A diffusion cell apparatus was used and the amount of drug permeated, diffusion and permeability coefficient through polymer membrane of various thickness were determined. As the polymer membrane thickness was increased, the diffusion and permeability coefficient was decreased. A modified surface tensiometer was used to measure the work of adhesion. As the drug or polymer level was increased in the formula, more force was required to detach the system from the mucus membrane of the rabbit. In general more force was needed to detach the system from the intestine than from the stomach tissue. Glipizide bioadhesive systems were successfully developed and evaluated. **Supported by INDUNIV GRANT**

A-70 **Prediction and Optimization of Theophylline Release From Hydrophilic Matrices.** **C.I. VARGAS * AND E.S. GHALY: School of Pharmacy, Medical Sciences Campus, U.P.R.**

The design and development of sustained release systems have become very interested in the pharmaceutical industries. In this study hydroxypropylmethylcellulose (HPMC) was used as the rate controlling polymer for theophylline release from tablet formulations. The factorial design was used and formulations containing different polymer levels (10% to 40% w/w) and different type of diluents (Lactose Fast Flo, Avicel PH-101 and Emcompress) were compacted into tablets by direct compression at a target weight of 450 mg and target hardness of 7-9 Kp. All tablet formulations were evaluated for physical properties and drug release. As the percent of polymer was increased from 10% to 30%, the drug release was decreased. However, there was no significant differences between tablets containing 30% and 40% polymer level. An equation was used to predict drug release from tablet formulations containing different HPMC levels using a limited number of experiments. Drug release data from dissolution experiments and theoretically calculated data were compared. It was found that the experimental data (from dissolution testing) match the predicted data very well. This approach can be applied to optimize the hydrophilic polymer level in the formulation design of hydrogel delivery systems using only a minimum number of experiments.

A-71 Effects of Valeriana officinalis Extract on GABAergic Transmission. J. Nieves, J. G. Ortiz Department of Pharmacology, and P.I. Chávez School of Pharmacy, Univ. of Puerto Rico Medical Science Campus, PO Box 365067, San Juan, P. R. 00936-5067

Gamma-aminobutyric acid (GABA) has been implicated as an important neurotransmitter in the mechanism of action of many anticonvulsants and sedative-hypnotics. Valeriana officinalis is classified as a garden heliotrope used as antispasmodic for convulsion, and as a sedative by folkloric medicine. Valeriana officinalis has been studied for its Central Nervous System activity and for its major constituents (Santos et al., 1994, Cavadas et al., 1994). We studied the effects of two different valerian extracts on GABAergic transmission. Synaptosomal [^{3}H]GABA uptake, [^{3}H]flunitrazepam binding and [^{3}H]GABA release assays were done to show this activity. Crude ethanol extract were synthesized using dried roots, aqueous extract were commercially obtained. Crude ethanol extract was capable of completely inhibit [^{3}H]GABA uptake while potentiation of [^{3}H] flunitrazepam binding was observed, both effects were dose- dependent. Commercially available aqueous extract showed to increase [^{3}H]GABA release, [^{3}H]GABA uptake was inhibited but to a lesser extent than crude ethanol extract. These observations point to Valeriana officinalis as a plausible GABAergic agent.
(Supported by the NIH/MBRS Program)

A-72 Regulation of Glutamate Transporter Activity by Second Messenger in Hippocampal Slice. O.Claudio and J.G.Ortiz Department of Pharmacology, University of Puerto Rico School of Medicine, P.O. Box 365067, San Juan, Puerto Rico 00936-5067

Glutamate (Glu) uptake is the primary process for its removal from the synaptic space. Nitric oxide, arachidonic acid (ARA) and G-proteins have been identified as possible regulators of Glu transporters. Previous studies had pointed out to alterations in Glu uptake and its regulations in several experimental epilepsy models. In synaptosomes, metabotropic Glu receptors (mGluRs) are possible source of the G-protein regulation of Glu transporters. Hippocampal slices have been extensively used in long-term potentiation and epileptiform activity studies. We used hippocampal slices in an attempt to clarify whether epileptiform activity was directly responsible for the changes in the activity of the Glu transporters. Rat hippocampal slices were pre-incubated for 1 hour with veratridine, 50 mM K^+, or reduced Mg^{+2}, as to mimic sustained depolarization; with ARA or metabotropic agents (MCPG or L-AP-4) to activate the G-protein regulation; or with the combination of depolarizing stimulus and the secondary messenger, to assess the effect of sustained depolarization on Glu transporter regulation. After the pre-incubation, the external medium was replaced by normal medium and Glu uptake assessed. With the exception of veratridine, none of the depolarizing stimuli had any effect on 5 μM or 50 μM [^{3}H] Glu uptake. ARA and the mGluRs agents, MCPG and L-AP-4 increased 5 μM Glu uptake, but had no effect on 50 μM. ARA, MCPG and L-AP-4 prevented to varying degrees, the decrease in 50 μM Glu uptake caused by veratridine. However, 50 mM K^+ and this agents are co-incubated, only ARA had any effect on Glu uptake. These results indicate that Glu uptake decreases under certain conditions of sustained depolarization (veratridine) and that ARA and mGluR agents may be useful in reversing such decrease. This approach may be useful in designing pharmacological strategies involving regulation of Glu transporters and in certain types of epilepsy.
(Supported by the institutional NIH/MBRS Program)

A-73 **Inhibition of Tyrosinase by Plants of Middle America.** **J. FERNANDEZ, R.O. GUERRERO[1], A. GUZMAN[2], and L.M. RODRIGUEZ[3]. [1]School of Pharmacy, UPR; [2]San Juan B. S. of Medicine; [3]CICY, Mérida, México.**

Tyrosinase is a copper containing enzyme that catalyzes several steps in the biosynthetic pathway of the melanin pigment. Tyrosinase inhibitors have become increasingly important for cosmetic and medical reasons, primarily in relation to hyperpigmentation. One hundred and twenty four plant extracts were analyzed for tyrosinase inhibition using a colorimetric assay. Fifty plants were collected in Puerto Rico, fifty in the Interandean and Amazon regions of Ecuador, and twenty four were procured in Yucatán, México. The assay was performed as previously described in the literature. A tyrosinase solution and phosphate buffer with and without the test sample were mixed and incubated at 25°C for 10 minutes. Then, one ml of DOPA solution was added. After incubation at 25°C for 2 minutes, the amount of dopachrome was measured at 475 nm. With these data, the percent of tyrosinase inhibition can be calculated. In general, the plant extracts showed mild inhibitory activity. Dalbergia monetaria from Puerto Rico and Brownea ariza from the Amazon basin exhibited the highest inhibitory action with 66% (IC_{50} 0.5693 mg/ml) and 63% (IC_{50}0.9632 mg/ml), respectively. It is hoped that the positive results of this study will be an incentive to continue analyzing the active principles of these species. The authors acknowledge the economic support of "Proyecto Farmacia", McNair Program, and the San Juan Bautista School of Medicine. The assistance of the "Instituto de Ciencias Naturales" of the "Universidad Central del Ecuador" in the procurement of some plant material is recognized.

A-74 **Controlled Release Theophylline Matrices Prepared By Using Carrageenan Polymer.** **N. RIVERA * AND E.S. GHALY ; School of Pharmacy, Medical Sciences Campus, U.P.R.**

Controlled release drug delivery design involves the application of physical and polymer chemistry to dosage form design to produce a well characterized and reproducible dosage form that control drug entry into the body within the specifications of the required drug delivery profile. The objective of this study was to prepare a sustained release matrix using carrageenan polymer as a retardant material and the direct compression method. The drug model selected for this study was theophylline. The different matrices were prepared by blending the polymer with the drug , excipient and lubricant. The excipients used were dibasic calcium phosphate, lactose fast flo and microcrystalline cellulose. The percent of drug was held constant (10% w/w), the percent of polymer was 10%, 30% or 40% and magnesium stearate (1%) was used as lubricant and the remainder was excipient. The dissolution data indicated that tablets prepared with 10% polymer and lactose fast flo released 94.1% of the drug; tablets prepared with 30% polymer released 59.2% and tablets prepared with 40% polymer released only 48% after 180 minutes. The drug release from hydrophilic swellable matrices decreased as the polymer level increased in the formula. The drug release from the prepared matrices was dependent on the polymer level and on the type of excipient used. Carrageenan can be successfully used as a retardant material for sustaining the drug release of direct compressed matrices.

A-75 **Cyanamide Increases Preference for Low Ethanol Concentrations in High Alcohol-Sensitive (HAS) Rats.** *B. Hine, J-C. Derieux.* School of Pharmacy, University of Puerto Rico.

We use rats selectively-bred for differential sensitivity to ethanol's (ET's) hypnotic effect (U. of Colorado) to study relationships between ET sensitivity, drinking and other variables. Our studies have shown that HAS males avoid or drink <1 g/kg/day of 10% ET in ET/water preference tests (PT), and treatments reported to increase ET drinking, such as low-dose opiate injections, are ineffective in these rats. We evaluated whether the aldehyde dehydrogenase (AD) inhibitor cyanamide (CY), which has produced conflicting data in ET intake studies, would increase intake using a PT with daily

increases in available ET concentrations (3-15%) and an injection dose regimen (10 mg/kg sc., b.i.d.for 3 days), reported to reliably increase ET intake in unselected rats by 2-5X control values. No difference in intake or preference occurred in 10 saline vs. 10 CY-injected rats previously matched for water intake. However, doubling CY injection doses and reducing injection-testing time to 6 days, 50 days later, resulted in more than a 2-fold increase in intake and preference for ET over the range of 4-9% ET, relative to saline-injected controls ($p<0.05$), despite some signs of toxicity in CY rats. HAS rats could have low basal AD and/or endogenous amine levels, thus limiting the hypothesized formation in the brain of condensation products, which increase ET drinking when administered to rats and are proposed by some to be involved in ET abuse.

A-76 Azidothymidine Triphosphate Characterization by Micellar Electrokinetic Capillary Chromatography.
J. BLOOM*, J. ORTIZ*, and J. F. RODRÍGUEZ#, School of Pharmacy*, School of Medicine#, University of Puerto Rico-Medical Sciences Campus.

There is a need to perform pharmacokinetic studies in the pediatric population utilizing antiretroviral drugs, which have shown effectiveness for the treatment of human immunodeficiency virus (HIV). In order to establish a relationship between efficacy and toxicity in children, we need to detect and quantitate these antiretroviral nucleotides and their metabolites using methods able to perform intracellular measurements. Capillary electrophoresis (CE) was investigated for the separation of five triphosphate nucleotides (CTP, ATP, TTP, GTP) including AZT-TP using micellar electrokinetic capillary chromatography (MECC). Fentomolar amounts of these nucleotides were satisfactorily resolved in 15 min. High peak efficiency and short run times (within 20 min) were obtained. In addition, only nanoliters of sample volume were used to perform the analysis using UV detection at 254 nm. We demonstrated that this technology is efficient in order to separate triphosphate nucleotides in a sample. The use of a small volume of sample decrease the amount of sample needed in order to perform pharmacokinetics studies in children under AZT treatment or other nucleoside-like antiretroviral drugs.

A-77 **Expression of Glutathione S-Transferase π in Human Lymphocytes from Type I Diabetic Patients**
Santiago, F. Aguiló, B.D. Jiménez. Schools of Pharmacy and Medicine, MSC.

High expression of Glutathione S-transferase (GST) Pi has been reported in preneoplastic lesions and used as a biomarker in rat hepatic tissue. In addition, a reduction in GST enzyme activity has been found in the liver of diabetic rats. Since several studies have shown the presence of this enzyme in human lymphocytes, we asked the question of whether this activity is also reduced in type I diabetic patients lymphocytes. Blood samples from type I diabetic patients were obtained and peripheral blood mononuclear cells (PBMC) were isolated. Western blots and GST enzyme assays were used to determine the concentration of GST Pi in the cytosolic fractions of PBMC. A significant reduction on GST Pi concentration (34% reduction) was found in lymphocytes from diabetic patients when compared to controls. We suggest that insulin might be directly or indirectly involved in the regulation of cytosolic GST. This is supported by previous studies in which GST Pi mRNA levels are elevated after insulin treatment in a specific human keratinocyte cell line.

A-78 **Effects of calcium-related agents on cytochrome P4503A1 expression in primary rat hepatocytes** AM Aviles[1], S Brown[2], PS Guzelian[2] and B Jiménez[1]. [1]University .of Puerto Rico, School of Pharmacy, San Juan, PR and [2]University of Colorado, Health Sciences Center, Denver, CO.

The induction of rat liver cytochrome P4503A1 (CYP3A1) gene produced by glucocorticoids and antiglucocorticoids is now known to be regulated by a mechanism different from the classical mechanism of glucocorticoid-responsive genes. Understanding details of the mechanism of CYP3A1 gene regulation will contribute to expand our knowledge in the regulation of genes by steroid hormones. Moreover, since cytochrome P450s are mainly involved in drug metabolism, this can be an important tool to understand drug interactions and adverse effects. In the present study, we evaluated the effects on CYP3A1 gene using several agents that alter the intracellular concentration of free calcium in primary rat hepatocytes. Total RNA was isolated from rat hepatocytes after they were exposed to a calcium agonist (A23187, Ouabain, Maitotoxin or Ciguatoxin) or a Calcium antagonist (Verapamil or Diltiazem) at various concentrations. The effects on CYP3A1 expression were evaluated by Northern blot hybridizations with a cDNA probe specific for CYP3A1 mRNA. The data obtained from Northern blot hybridizations showed a reduction in CYP3A1 mRNA levels when rat hepatocytes were exposed to low concentrations of calcium agonists and high concentrations of calcium antagonists. A marked reduction was observed with the calcium agonist A23187. These results suggest a possible role of calcium in the regulation of this gene, where a high level or a very low level of calcium in the cell may be involved in the control of CYP3A1 gene expression. How a specific concentration of intracellular calcium affects the regulation of the CYP3A1 gene and the intermediate(s) involved in this mechanism need to be determined.

A-79 **Relation Between Joint Sounds and Bone Erosion in TM Joints.**
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TM tomography can help to detect changes on condylar surfaces which have been related to TM disorders. Advances in TM sonography have been utilized to identify TMD conditions by studying the characteristics of recorded sounds. This study will try to correlate changes occuring on condylar surfaces with sounds recorded from the same TM joints. Two groups of patients, twenty two TM patients who reported joint sounds and 14 non TM patients (control group) had tomograms (Denar Quint Sectograph) and TM sonograph recordings (MYotronics) of right and left joints. A radiographic index (0=no erosion to 3=erosion on 3 surfaces) was compared to a sound index (0=no sound to 3= crepitus). The data obtained was analyzed utilizing a non parametric test (McNemar, sspsx) to test the null hypothesis of both test groups. For both right and left joints respectively, X=.188, X= .439. It was found to be not significant at the .05 level. In con-

clusion, tomographic and sonographic tests alone cannot be utilized to obtain a proper TMD diagnosis, but they remain as useful adjuncts to traditional diagnostic data gathering.

A-80 The Role of Metal Alloys in the Pathogenesis of Oral Mucosal Lesions and the Burning Mouth Syndrome. Julia de Hernández C*, Sánchez JL, Ortiz A., University of Puerto Rico, School of Dentistry and University of Puerto Rico, School of Medicine, San Juan, Puerto Rico

This study is part of a wider clinical investigation on the diagnosis and treatmemt of contact allergic reactions to dental restorative materials. Fifty patients with cast metallic restorations who complained of burning sensations of the mouth, dryness of lips, unpleasant metallic taste and redness of the oral mucosa, were studied. A detailed history, oral examination, laboratory tests, radiographs, patch tests and soft tissue biopsy were the diagnostic procedures used with each patient. Information of brand names and composition of the alloys was obtained to establish clinical relevance of positive patch tests to the component metals of the alloys. Examination of the oral mucosa, revealed areas of erythema, edema, erosions, lichenoid changes and either atrophy or inflammation of tongue papillae. Laboratory tests and radiographs ruled out other oral diseases. Patch tests to one or more metallic substances were positive in 36 patients. The histopathological findings were epithelial spongiosis and a mixed-cell inflammatory infiltrate of lymphocytes, plasma cells and eosinophilis. The clinical relevance of positive patch tests was established in 28 cases by correlating them to the physical and histophathological findings and to the component metals of the alloys present in the restorations.

A-81 Cross-reactivity between *Dermatophagoides pteronyssinus* and *Blomia tropicalis*. C.I. MORA*, F. MONTEALEGRE and A.M. DIAZ. School of Medicine, Medical Sciences Campus, UPR and Ponce School of Medicine.

The objective of this research was to define species-specific and cross reactive antigens from the house dust mite *Dermatophagoides pteronyssinus* (DP) and the storage mite *Blomia tropicalis* (BT). To this end, polyclonal antibodies to whole mite body extracts from DP and BT were produced in rabbits. The homologous and heterologous reactivity from the obtained antisera were tested by ELISA and the specific and cross-reacting antibodies were detected by Western blots.

The results show that these mites contain multiple antigens, some of them are shared by DP and BT and other ones are specific to each mite.

The results of this study have considerable implications for the diagnosis, management and epidemiology of mite mediated allergies, as well as for mite and allergen production for use in immunoassays.

A-82 ***Compliance of HIV+ Injection Drug Users to Clinical Trials Protocol Mandated Evaluations at the University of Puerto Rico Adult ACTU*** G.J. VAZQUEZ; M. CRUZ-ORTIZ; S.I. DAVILA; I. LOPEZ; V. RAMIREZ. UPR School of Medicine, UPR Adult ACTU/Site 5401.

The Adult AIDS Clinical Trials Unit (ACTU) of the University of Puerto Rico, School of Medicine is an NIAID sponsored facility that provides clinical research protocols in HIV/AIDS and its complications to voluntary participants. It has been subjected that compliance of Injection Drug User (IDU) in study protocol has been very disappointing. The purpose of this study is to identify differences with regard to their compliance to protocol mandated evaluations between the Injection Drug Users and those other participants not associated with Injection Drug Use (N-IDU). The medical records of all participants recruited to protocols from May, 1992 to August, 1996 were retrospectively reviewed and statistical analysis was performed utilizing Pearson's Chi-Square. As of August 1996, 208 subjects have been enrolled into different protocols, 139 (67%) males and 69 (33%) females. IDU was reported in 49 (24%) of the participants 40 males and 9 females. No statistical differences was noted when the two groups were compared using protocol specific criteria as to be off study such as: protocol completion (IDU:32% vs N-IDU:41%); death (IDU:24% vs N-IDU:14%); treatment termination (IDU:51% vs N-IDU:61%). A higher rate of missed visit was observed in the IDU's group (53%) than in the N-IDU's (37%) this differences was not marginally significant. In conclusion, both the IDU and N-IDU groups were comparable in their compliance of protocol mandated activities, suggesting a similar behavior pattern in both groups.

A-83 Sensitivity and Specificity of Two Hybridization Methods for the Screening of a T. gondii cDNA Library for Pyrimidine Biosynthetic Enzymes. MARIA L. SIERRA-PAGAN and BARBARA H. ZIMMERMANN. Department of Biochemistry, Univ. of Puerto Rico, Medical Sciences Campus.

Toxoplasma gondii is a protozoan parasite that severely affects immunocompromised patients. Current treatment involve the administration of a combination of pyrimethamine and sulfapyrimidine. Unfortunately these drugs can not be administered for prolonged periods of time due to their extreme toxicity to the cells, therefore an alternative treatment is needed to reduce the severity of the disease. To evaluate the potential of the parasite's pyrimidine biosynthetic pathway as target for chemotherapy, the enzymes involved must be isolated and studied. Two hybridization methods were evaluated to determine

which one was suitable for the identification of underrepresented sequences in a cDNA library. One of the methods is based on the formation of a biotin-streptavidin-phosphatase complex and the other is based on the detection of beta emission upon hybridization of targets to a 32P labeled probe. To standardize the hybridization conditions for the assays the antigen p30 and the dehydrofolate reductase sequences were used as targets; these proteins represent a range between high and low cDNA copy numbers. Results showed that the non radio-active based method is sensitive but is not specific enough to be used to screen a cDNA library, therefore the radioactive based method will be used to isolate the cDNA clones that correspond to the pyrimidine biosynthetic enzymes. (Support provided by RCMI #G12RR03051 and MBRS S06GM08224.)

A-84 Effect of Ascorbic Acid on Plasma Glutathione levels in HIV Seropositive Pediatric Patients

Shirley Gonzalez, MD, Ibet Heyer, RN, Joel Cordero, Jose Rodriguez Orengo, Ph D, Clemente Diaz, MD

The factors which determine the period of latency of HIV are not completely understood. Cytokines, NFkB and redox status, all seem to play a role. Glutathione (GSH), a major reducing agent in the body, may play a role in keeping the HIV in latency. In vitro studies have shown that GSH has a suppressive effect on reverse transcriptase. (Kalebic, T, et al, 1991) **Objective:** To study the effect of a reducting agent, Ascorbic acid, on GSH levels in HIV seropositive pediatric patients. Studies done on newborn rats and on guinea pigs treated with Ascorbic acid, demonstrated a sparring of GSH. (Mrtensson, J, et al, 1991) HIV infected cells exposed to Ascorbic acid had decreased reverse transcriptase activity and p24 expression. (Harakeh, S, et al, 1991) **Methods:** Twenty-four patients were enrolled in this study. (age=33-181 mo.) GSH levels were measured before and after Ascorbic acid administration (pc). **Results:** Mean GSH levels before and after Ascorbic acid, did not change, (2.82 uM and 2.72 uM, respectively). GSH levels were measured in plasma using High Pressure Liquid Chromatography. Mean GSH level was lower than that observed by Smith, CV, et al, 1991, in plasma of newborn infants (3.5-1.4 uM) and in healthy adults (7.2-0.2 uM). **Conclusions:** Future studies are needed to investigate agents which could increase GSH levels in HIV seropositive pediatric patients and to their effects on clinical manifestations and virus replication. Higher doses of ascorbic acid in future clinical trials would be warranted.

A-85 Jacalin-Induced Apoptosis in Cultured PBLs from HIV+ Subjects is Reduced by Nitric Oxide Synthase Inhibitors.

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Jacalin (JAC), a lectin mitogenic for T lymphocytes has been reported to block in vitro HIV infection of human CD 4 + lymphocytes (Favero et al., 1993). The proliferative responses and the apoptosis (A_o) induction of lymphocytes cultured with this lectin were studied in fifty samples from HIV + patients and compared to those of ten uninfected subjects. These effects were assessed by flow cytometry and compared to those of PWM- and PHA - stimulated PBLs. Among uninfected subjects, PHA stimulation resulted in the highest proliferative response followed by PWM and JAC, while no mitogen induced A_o. In contrast, HIV + patients showed decreased proliferation responses with the three mitogens when compared to normal values, and their unstimulated PBLs exhibited low percent values of spontaneous A_o (21.6 ± 10.4) which increased by stimulation with PWM (25.4 ± 13), JAC (29.1 ± 12.8) and PHA (34.2 ± 15.5). PBLs were also cultured in the presence of N-Monomethyl-L-arginine (L-NMMA) and 7-Nitroindazole (7-NI), two nitric oxide synthase inhibitors, resulting in a significant inhibition of A_o. The percent of inhibition with L-NMMA in JAC-stimulated PBLs was highest (67.3 ± 15.6; 36.7 ± 19.3 with 7-NI), followed by PHA-stimulated PBLs (61.9 ± 13.4) and PWM-stimulated (42.4 ± 20.4). These results indicate that JAC is a potent inducer of apoptosis in cultured PBLs from HIV + patients. This phenomenon is reduced by L-NMMA and 7-NI, supporting the role of NO in apoptosis induction in this model Supported by RCMI-RR03051.

A-86 **Three Puerto Rican Children with Growth Hormone Deficiency-like State Secondary to Psychosocial Short Stature.**

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Classic growth hormone deficiency (GHD) is characterized by growth failure and blunted GH secretion to either physiological or pharmacological stimuli. This GHD is usually a life-long permanent deficiency. On the other hand, psychosocial short stature (PSS), is the only known cause of reversible GHD. Herein we present three cases of children evaluated at the University Pediatric Hospital because of growth failure (see table).

Case	CA[1] (yrs)	Ht.[2] (cm)	HA[3]	Wt.[4](Kg)	BA[5] (yrs)
JCN	15.5	132.1	8.8	26.4	10.0
PJF	6.4	97.6	3.3	14.1	4.5
VPD	4.5	80.0	1.2	13.5	2.0

[1]CA, chronological age; [2]Ht., height, [3]HA, height age; [4]Wt., weight; [5]BA, bone age

All of them demonstrated a GHD as determined by their growth hormone production after pharmacologic stimulation (i.e., peak level < 10μg/L). Medical evaluation excluded organic causes for growth failure. However, psychosocial evaluation revealed the presence of psychosocial harassment by caretakers and the subjects demonstrated a bizarre behavior such as going through trash for food. These findings prompted evaluation toward the possibility of PSS. Thus, they were removed from their caretakers homes and placed in foster nurturing environments. Once relocated, the three children were able to demonstrate marked weight gain, growth acceleration, and improved social behavior. These changes were accompanied by biochemical evidence of GH-axis recovery as determined by the augmented insulin-like growth factor I levels and GH secretion. Although rare, these results were felt to be most compatible with PSS, the only known cause of reversible hyposomatotropism. In summary, we present three cases of children with a GHD-like state secondary to PSS. We conclude, that infants and children with growth failure, who do not have an organic cause for this, should be suspected of having PSS. Early interdisciplinary evaluation is key for a successful outcome.

A-87 **Microphallus and Hypoglycemia: Hallmark of Hypopituitarism in the Newborn Period.**

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Although rare, hypopituitarism should be suspected in newborns with midline defects. Some of these defects may be subtle enough that time could unduly

pass before being recognized. We present a term infant born after uneventful pregnancy, who at birth was noticed with small genitalia and at 24 hrs of age developed generalized seizure with central glucose level of 24 mg/dl. The patient was transferred to the Universitary Pediatric Hospital for evaluation. Examination on arrival was significant for coarse features and small phallus of 1.5 cm x 0.4 cm with descended testicles. He was unable to control body temperature requiring incubator care and demonstrated poor sucking. At 8 day old, he developed an episode of profound hypoglycemia with a central glucose of 0 mg/dl. Laboratories during spell demonstrated failure in counter regulation, growth hormone < 1.0 µg/l and cortisol 0.27 µg/dl. Insulin serum levels were diminished (2.3 µU/ ml). He also presented hyponatremia (122 mEq/L), hyperkalemia(7.6 mEq/L), and hypothyroxinemia with low thyrotropin serum levels (T_4 1.42 µg/dl, T_3 U 29.7%, FTI 0.48, TSH 0.42 µIU/ml). He required 12 mg/Kg/min of parenteral glucose continuous infusion to prevent hypoglycemia before starting hormonal replacement. These results were felt to be compatible with hypopituitarism for which replacement with growth hormone, cortisol, and levothyroxine was initiated with rapid normalization of the metabolic derangement. A head CT scan showed normal size of the sella turcica without evidence of hemorrhage. In summary, we present a newborn male with microphallus, as a midline defect, and hypoglycemia caused by hypopituitarism. The early recognition and treatment of hypopituitarism during neonatal period is essential to prevent from irreversible devastating neurological sequelae hypoglycemia may produce.

A-88 Di George Sequence in a preterm newborn.

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Di George sequence refers to absence or hypoplasia of the thymus and/or parathyroid glands with cardiovascular anomalies, especially interrupted aortic arch and truncus arteriosus, and various craniofacial abnormalities. Incidence is 1:66,000 and more than 90% of the cases have a deletion 22q11.2. We report a baby boy preterm adequate for gestational age born to a 15 y/o G1P0A0 mother with no history of systemic illness via vaginal delivery at 34 4/7 weeks of gestation. Mother denies exposure to alcohol, nicotine, retinoic acid, vitamin A derivatives, or other drugs. Apgar score 5/7 at 1 and 5 minutes respectively. Birth weight 1450 grams. Patient was admitted to NICU requiring mechanical ventilation. Esophageal atresia with distal tracheoesophageal fistula and annular pancreas were diagnosed and repaired at two days old. An echocardiogram was done that showed patent ductus arteriosus, patent foramen ovale, and left aortic arch. At 3 day/old the patient developed hyponatremia, hypocalcemia, and thrombocytopenia. Serial chest x-rays showed absence of thymus shadow. The patient developed intraventricular hemorrhage with hydrocephaly requiring a ventriculoatrial shunt. Intact parathyroid hormone levels were reported < 3 PG/ml N(11-54), calcium 6.9 mg/dl results compatible with primary hypoparathyroidism. Chromosomes with fluorescent in situ hybridization were reported as 46XY del 22q11.2. Hospital course was complicated with cerebrospinal fluid infection and septicemia secondary to Enterobacter Cloacae. The patient subsequently developed multisystemic failure which lead to his death at 2 ½ month of age. Hypocalcemia and absence of thymic shadow in a premature newborn should alert the clinician to the possibility of Di George sequence.

A-89 Neonatal Candidiasis: High index of suspicion.

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Disseminated fungal infections, previously rare, are now frequently diagnosed in neonatal intensive care units. This increasing incidence correlates with the improved survival of the very low birth weight infant. Factors responsible for this increased incidence are the use of: broad-spectrum antibiotics, prolonged endotracheal intubation, use of theophylline for apnea of prematurity, and indwelling arterial or central venous catheteterization. Candida albicans is implicated in 80% to 90% of human fungal infections and is responsible for 75% of neonatal infections. It occurs in 2% to 4% of very low birth weight infants. Presentation typically occurs at an approximate age of 5 weeks. Previously the diagnosis was not made until autopsy in 30% of neonates. Since laboratory confirmation of infection is difficult, the clinician must maintain a high index of suspicion. We report a 2 months old male twin #2 born to a 22 years old G2P1A0 mother, with history of pre term labor and pneumonia. The mother had PROM with suspected chorioamnionitis. The patient was born at 28 weeks of G.A. via cesarean section due to transverse presentation and failed tocolysis. He required orotracheal intubation due to respiratory distress, APGAR 7/8 at 1 and 5 minutes respectively, BW 1Kg. The patient's initial problems were: HMD treated with 1 dose of Survanta, PDA treated with Indocin, Hyperbilirubinemia without incompatibility treated with phototherapy for 4 days, IVH grade 4 with Leukomalacia at 7 day old. At 15 day old the patient developed persistent gastric residues and vomiting. Repeated blood cultures revealed Candida albicans for which the patient received 30 mg/Kg of total Amphotericin B therapy. No cardiac vegetations were found in an Echocardiogram, but an Abdominal sonogram showed hyperechoic lesions on liver and right kidney suggestive of fungal inflammatory process. Ophthalmology evaluation and cerebrospinal fluid had no evidence of infection. Considering that no prenatal or perinatal risk factors have being clearly defined, a high index of suspicion for early diagnosis is necessary. In view that the rarity of this disorder is being questioned, clinical investigation is needed to asses the incidence of intrapartum candidiasis and identify the predisposing factors that can make a premature newborn prone to develop congenital candidiasis.

A-90 Fluctuating Asymmetry in Babies Exposed to Cocaine or Cigarette Smoke in Uterus.

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Fluctuating asymmetry is a measurement used to indicate the degree of variability among symmetrical structures in an individual. Although it can be used as an index of developmental homeostasis, there are no reports where this tool has been used in humans to measure the extent of the detrimental effect of drugs of abuse during gestation. We decided to investigate if smoking or cocaine use during pregnancy had an effect on neonatal symmetry. Footprints were collected from babies of less than 24 hrs born in the San Juan Municipal Hospital. Urine samples were collected and assessed by radioimmunoassay for cocaine and nicotine. Left and right foot length, width and perimeter were compared with the assistance of an image analyzer (Imaging Research Inc.). Nicotine and cocaine increased fluctuating asymmetry of feet perimeter, nicotine having a greater effect. No effect was observed in feet length and width, which are linear measurements. This increase in fluctuating asymmetry suggest

that many internal processes that regulate homeostasis during development may also be affected. This work was supported in part by an Institutional grant from the Associate Deanship for Graduate Studies and Research of the University of Puerto Rico, Medical Sciences Campus and by RCMI award RR-03051 for the development of a Clinical Research Center and for the Image Analysis Resource Center.

A-91 **Heterogeneous Nature of the [Ca]i Storage Site in Single Rat Hepatocytes. J. BERNSTEIN AND R. FURILLA. Dep. Physiology, Sch. Medicine, UPR.**

Isolated single hepatocytes loaded with Fura-2, mounted on poly-Lysine coated coverslips, were incubated in a Hanks modified medium at 37°C and pH 7.4. Thapsigargin, a well known inhibitor of Ca uptake by the endoplasmic reticulum, when used at 2 μM in a Ca-free medium, produced a peak showing a rapid increase in [Ca]i, followed by a plateau and a slower decrease. However, further analysis of the data obtained by Baffy et al, J. Cell Physiol. 153: 332-339 (1992), by using a powerful peak-fitting algorithm (Peak Fit v 3 , Jandel), showed the existence of 3 distinct peaks each best described by Asymmteric Double Sigmoidals. The first peak was centered at 22.6 sec with an amplitud of 80.9 nM [Ca]i (net change), representing about 3% of the released Ca; its sigmoidal rate of release was 0.0237 sec. The second peak was centered at 31.59 sec with an amplitude of 208.88 nM [Ca]i, representing about 68% of the released Ca; its sigmoidal rate of release was 1.58 sec. The third peak was centered at 101.31 sec with an amplitude of 79.31 nM [Ca]i, representing about 30% of the released Ca; its sigmoidal rate of release was 18.99 sec. In addition, the results also show 3 distinct processes for cytosolic Ca extrusion different from endoplasmic reticulum uptake showing sigmoidal rates of 5.63 sec, 11.41 sec and 12.84 sec, respectively. Further identification of these compartments may be essential to understanding hormonal action.

A-92 **Epilepsy Induces Alteration in Opioid Immunoreactivity of Hippocampal Neurons in Epileptic Patients.** C.A. Mejías, J.A. Inserni and A.C. Segarra. U. of Puerto Rico, Depts. of Neurology and Physiology, Medical Sciences Campus.

Next to strokes, epilepsy is the most common neurological disease, affecting approximately 1% of the population. It results from an abnormal discharge of cortical neurons. These discharges produce stereotyped and involuntary movements and even loss of consciousness. Patients that are refractory to pharmacological treatment are evaluated for surgical removal of the epileptogenic region as a therapeutic procedure to relieve complex partial seizures. The main objective of this study is to investigate if changes in the endogenous opioid system are associated with temporal lobe epilepsy. Hippocampi excised from 2 epileptic patients, one with cryptogenic intractable temporal lobe epilepsy and one with a temporal lobe tumor were examined for the presence and distribution of immunoreactivity for endogenous opioids. These hippocampi were compared to hippocampi from fresh cadavers. In the control hippocampus, the order of immunoreactivity was as follows: dynorphin > met-enkephalin > leu-enkephalin. The hippocampus excised from the cryptogenic patients exhibited an increase in met-enkephalin and a decrease in dynorphin immunoreactivity, leu-enkephalin immunoreactivity was unchanged. Immunoreactivity in the hippocampus excised from the patient with a tumor showed no major difference from the control. These results suggest that opioids may be associated with the sclerosis exhibited in temporal lobe epilepsy. (This research was supported by RCMI G12 RR11126 and G12RR-03051, and the Deanship for Academic Affairs, UPR, MSC, CAM is a recipient of a Amer. Psychol. Assoc. Minority Fellowship).

A-93 **An Spatial Limited-Angle Model for X-Ray Tomography and Transmission Electron Microscopy.** Pablo M. Salzberg, Department of Mathematics and Computer Sciences, UPR-RP.

This contribution deals with the development of an spatial, limited-angle model for X-ray tomography, and for transmission electron microscopy. This model, which produces highly parallelizable reconstruction algorithms, is based on Radom transforms over finite fields. The heuristic for this algorithm was introduced by the author in connection with a technique (QUANTITEM) recently developed by Peter Schwander et al. at AT&T Bell Laboratories, which allows to count approximately the number of atoms in each atomic column of a crystal, in case that there is only one type of atom. From the knowledge of the approximate number of atoms in each atomic column along a small set of directions, obtained by tilting the crystal, our tomography model can be used to reconstruct the atomic configuration of the crystal lattice. We shall exhibit some reconstructions for simulated X-ray tomography and electron microscopy performed by these algorithms.

This research has been supported by MBRS-NIH Grant S06GM08102, and by the AT&T Foundation.

A-94 Cell death in the retina after axotomy and rescue by bFGF. BLANCO, R.E. Institute of Neurobiology and Department of Anatomy, Medical Sciences Campus, University of Puerto Rico.

In the case of the mammalian optic tract, cutting the optic nerve behind the eye leads to limited regenerative attempts at the lesion site, followed by death of more than 90% of retinal ganglion cells by one month after axotomy. The regenerative capabilities of the CNS of lower vertebrates such as fish and amphibians are well known. When the optic nerve of the leopard frog, *Rana pipiens* is severed, it can regenerate and eventually form functional connections. Despite this

regeneration, Nissl staining of the retina shows a striking decrease in the number of cells in the ganglion cell layer 6 months after axotomy. Experimental retinas at 6 weeks after axotomy contained dying cells, the majority of which had pyknotic nuclei. Six months after axotomy, no pyknotic nuclei were seen but some cells contained what appeared to be apoptotic bodies, evidence of programmed cell death. A study of the density of cells in different regions of the retina showed that, despite the normal regional differences in density, less than 50% of the ganglion cells were still present 26 weeks after the nerve was cut. In contrast with the rat, 4 weeks after axotomy cell death is less than 10% in some areas, while in others there is no significant decline in density. By 6 weeks the density of cells has declined on average by 13% compared to controls. Addition of basic fibroblast growth factor (bFGF) to the optic nerve stump virtually eliminated this decrease 6 weeks after axotomy. (Research supported by CIDIC-RCM institutional grant and NIH-MBRS RFA GM-96-008 GM-RR-03051)

A-95 Depression and Paired-Pulse Facilitation of EPSP Amplitude during Embryonic Development in the Cercal Sensory System of the Cockroach. M.A. Sosa and J.M. Blagburn. Institute of Neurobiology and Depts. of Anatomy and Physiology, University of Puerto Rico Medical Sciences Campus.

The cerci of the first instar cockroach (*Periplaneta americana*) bear two filiform hairs each, one lateral (L) and one medial (M), which are innervated by individual sensory neurons. These sensory neurons project to the central nervous system, where they synapse with giant interneurons (GIs) in the terminal abdominal ganglion. Cockroach embryos kept at 30°C take approximately 30.5 days to develop and hatch. The synapse between L and the contralateral GI3 forms between embryonic days 16 and 18. Here we characterize some of the properties of this synapse as it develops, specifically the phenomena of depression and short-term facilitation of excitatory postsynaptic potential (EPSP) amplitude. Intracellular recordings of contralateral GI3 EPSPs, in response to direct electrical stimulation of L, were made in 16-23 day old cockroach embryos. The L-GI3 synapse of first instar nymphs is known to normally operate at a depressed level. Estimates of this steady-state level of depression were made for the embryos by stimulating L action potentials at a frequency of 2 Hz and measuring the GI3 EPSPs. Once a steady EPSP amplitude was reached, L was stimulated with pairs of pulses delivered at the same frequency. Paired-pulse facilitation was estimated at different stimulus intervals. We have found that both depression and paired-pulse facilitation are present from when the L-GI3 synapse is first formed. However, while depression of EPSP amplitude (at 2Hz) stays relatively constant throughout embryonic development, facilitation was larger initially, during embryonic days 16 to 18. Afterwards, it remained relatively constant at a smaller level, at least up to day 23. These results indicate that the transmitter release machinery required for depression and short-term facilitation are present immediately upon formation of a functional L-GI3 synapse. Supported by NIH Grant NS07464, with additional support from NIH RR03051 and an NSF Minority Postdoctoral Research Fellowship.

A-96 The Importance of Target-derived Factors in Directing the Precision of Motor Axon Regeneration

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The axons of a severed peripheral nerve grow across a gap in their pathway to regenerate into the distal nerve stump. At the turn of the century this observation led Cajal to propose that concentration gradients of factors released from the cells of the distal nerve segment orient the growth of the regenerating axons. Results from *in vivo* experiments subsequently showed that diffusible factors released from the sectioned peripheral nerve play a role in directing regenerating motor axons, however, the mechanism by which they worked were not clear. Recently, several central nervous system target-derived factors have been shown to direct process outgrowth *via* concentration gradients of the factors during development. It has also now been shown that concentration gradients of a severed peripheral nerve-released factor/s can direct the outgrowth of growth cones of adult sensory neurons *in vitro*. A conclusive demonstration of concentration gradients of peripheral target-derived factors directing the outgrowth of adult motoneuron growth cones has remained elusive. We examined whether concentration gradients of diffusible factors released by the cells of a length of peripheral nerve influence the outgrowth of growth cones of adult motoneurons *in vitro*. We demonstrate that the growth cones turn and grow up the concentration gradients and this influence was effective over distances of up to several hundred microns. Thus we have shown that diffusible concentration gradients of peripheral target-derived neurotropic factors can direct the regeneration of motor axons in the peripheral nervous system. Research supported by: ARO DAAL03-90-G-0189, ONR NB-91-12- I 0 1, NIH 5 PO I NS07464-25, NSF-EPSCoR EHR9108775, and DoD NOOO 14-93-1-13 80.

A-97

Trophic influences of muscle-derived factors on adult motor neurons *in vitro*

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The regenerating axon has several potential sources from which it can derive neurotrophic or neurotropic influences. The peripheral nerve, the ECM, and the muscle fiber itself are possible sources for these factors. For axonal regeneration to be successful the axon must be encouraged firstly to grow and secondly to grow in the right direction. Experiments have previously shown that peripheral nerve-derived factors are capable of doing both of the above. The present experiments were designed to assess whether a neurotrophic effect is exerted on motor neurons by diffusible factors released by the ultimate target of motor axon regeneration, the muscle fiber. Co-cultures with denervated, dissociated lumbricalis extensor muscle fibers and motor neurons (from adult Rana pipiens) were set up. The muscle fibers were pre-denervated 4 to 6 days prior to their placement in the co-cultures to allow for possible up-regulation of release of diffusible factors. Special chambers were desiged for the co-culture. Two pieces of teflon (90 um thick) serve as the walls of the chamber and a glass coverslip is placed on top. This design is advantageous in that the very small volume (ca. 2.5 mm^3) serves to.maximize the neurotrophic effect of putative muscle-derived factors, and the open-ended desgin allows for a minimal exchange of medium with the "external milieu" of the petri dish. Control motor neurons were cultured in identical chambers without muscle fibers. The motor neurons cultured with the muscle fibers have an increased average individual process length, a decrease in the average number of processes per neuron, and are morphologically distinct from the control neurons. Thus, the present experiments suggest that factors released from denervated, dissociated muscle fibers are capable of exerting neurotrophic influences on adult motor neurons.
Research supported by ARO DAAL03-90-G-0189, ONR NB-91-12-1 0 1, NIH 5 PO I NSO7464-25, NSF-EPSCoR EHR9108775, and DoD NOOO14-93-1-13 80.

A-98 Using λ-shaped Silicone Chambers to Study Axon Guidance *in vivo*

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We present an *in vivo* approach to studying the regeneration of cut nerves in the rat. It is known that axons are capable of growing along a concentration gradient of guiding (neurotropic) molecules *in vitro*. We developed a technique which presents regenerating cut axons in the live animal with two distinct options of growth directions: one with an established gradient of tropic factors, and one without a gradient. The sciatic nerve of adult rats was cut and introduced into a silicone chamber with λ-shaped tunnels and three outlets. To establish a concentration gradient inside the chamber a catheter carrying sciatic nerve conditioned medium from a mini-osmotic pump was introduced into the second outlet. The third outlet was left open. The chambers were analyzed after 25 days and stained with antisera against neurofilament protein to visualize the regenerated axon bundles. Preliminary results show that axon regeneration occurs preferentially in the tunnel of the chamber containing the catheter, requiring an active turn of more than 125° for the axons to grow into the short arm of the λ. This suggests that an effective guidance mechanism directs the regenerates along a concentration gradient of neurotropic factors. Experiments are currently under way to isolate and identify the factors responsible for this potent effect of attraction of regenerating nerves. Ultimately our techniques may have clinical relevance in improving nerve regeneration after injury.
Research supported by ARO DAAL03-90-G-0189, ONR NB-91-12-I 0 1, NIH 5 PO I NS07464-25, NSF-EPSCoR EHR9108775, and DoD NOOO14-93-1-13 80.

A-99 Polysynaptic inputs contribute to the receptive fields of GIs in the 1st instar cockroach

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The cercal sensory system of the first instar cockroach (Periplaneta americana) has two filiform hairs on each cercus, termed lateral (L)and medial (M). Each hair is associated with an individual sensory neuron. The neurons make connections with giant interneurons in the terminal abdominal ganglion. We were interested in determing whether indirect connections are present between the sensory neurons and GIs. The appropriate sensory neuron was stimulated by mechanically moving the filiform hair. Simultaneous intracellular recordings were made from a GI known to receive direct input from that sensory neuron, and from the GI under test. Criteria for determining the existence of an indirect connection were (1) lack of correspondence between spontaneous EPSPs in the reference GI and those in the test GI, and (2) a delay between the onset of the evoked responses in the two GIs. Physiological evidence suggests a strong indirect, excitatory connection between the contrlateral GI1. This completely alters its directional sensitivity, allowing it to respond to wind from the front contralateral quadrant as well as from the rear contralateral quadrant. An indirect excitatory connection was also found between the M sensory neuron and the ipsilateral GI5. GI6 and GI7 were found to receive indirect inhibitory input from the ipsilateral M, which would sharpen their receptive fields. These experiments have shown that filiform hair sensory input can reach the post-synaptic GIs via polysynaptic excitatory and inhibitory pathways. These inputs do not simply fine tune the receptive fields of the GIs, but may make an important contribution to their directional sensitivity.
Research supported NIH grant NSO7464, and an NSF EPSCoR grant.

A-100 Expression of Utrophin and Dystrophin A ssociated Glycoproteins in Muscle Biopsies from Patients with Dystrophinopathies in Puerto Rico.

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Dystrophin deficiency results in the disruption of the linkage between sarcolemmal cytoskeleton and a large oligomeric complex of sarcolemmal proteins known as Dystrophin-associated Glycoproteins (DAG). Adhalin and beta-dystroglycan, are integral proteins of the DAG complex which may contribute of the stabilization of the normal muscle membrane. Utrophin, a dystrophin homologue protein have been reported to be increased in dystrophin-deficient muscles. This suggests an up-regulating mechanism to compensate for dystrophin deficiency. We studied muscle biopsies of thirty-six patients patients with myopathies using immunocytochemical labelling for dystrophin. Three showed no positive staining for dystrophin, indicative of Duchenne Muscular Dystrophy (DMD) and other three had reduced immunoreactivity compatible with Becker Muscular Dystrophy (BMD). We compared the immunoreactivity distribution of adhalin, beta-dystroglycan and utrophin in muscles of five of these patients. Only one young adult patient (BMD) showed an increase expression of utrophin , which correlates with previously reported data. Other three patients in the ages of four or less did not exhibit increased utrophin immunolabelling. In addition, three cases did not show immunoreactivity neither for utrophin nor beta-dystroglycan These findings suggest that expression of utrophin may be dependent on the prescence of beta-dystroglycan and to the age of the patient. (Research was supported by RCMI G12 RR11126 and G12 RR-03051, and the Deanship Academic Affairs, UPR, MSC)

A-101 Isolation and Analysis of Rabbit Cardiac Muscle Thick Filaments.

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In spite of the importance of cardiac muscle, very little information is available on the detailed molecular structure of the cardiac muscle thick filament either from electron microscopy or X-ray diffraction studies of the living muscle. To elucidate the structure of these filaments, we have developed a procedure which allows the isolation of the cardiac thick filaments for study by electron microscopy. The isolated filaments appear periodic with a helical repeat every third crossbridge level (43 nm) as previously seen in isolated skeletal muscle thick filaments and consistent with the data from X-ray diffraction. The periodicity of the filaments has been confirmed by examining both optical diffraction patterns

and computed Fourier transforms of electron micrograph images of the filaments. These studies support three major conclusions: 1) The weakness of the layer lines in the X-ray diffraction patterns of heart is not due to an inherent disorder in the arrangement of the myosin in the cardiac thick filament. 2) The cardiac filaments differ from skeletal muscle thick filaments in their strong tendency to remain attached to actin under relaxing conditions. 3) The structure of the isolated thick filaments by image analysis is consistent with a three-stranded arrangement of the crossbridges on the filaments. This investigation was supported by a 'Research Centers in Minority Institutions' award RR-03051, from the National Center for Research Resources (NIH) and a Grant-in-Aid Award from the American Heart Association of Puerto Rico.

A-102 Head and Trunk Stabilization in Natural Gaits of Free-Ranging Monkeys. D.C. DUNBAR and G.L. BADAM: Dept. of Anatomy and Caribbean Primate Research Center, Univ. of Puerto Rico Med. Sch., San Juan, PR 00936; Deccan College, Pune 411006, India.

Are there restrictions on how the head-fixed vestibular apparatus can be positioned or reoriented via head movements without deteriorating the nervous system's perception of spatial orientation? If so, what are these restrictions? To address these questions, the natural walking and running behaviors of wild monkeys (Presbytis entellus) were cinefilmed at high-speed (100 frames/s). Kinematic analysis focused on angular movements of the head and trunk relative to absolute space (earth-horizontal reference). During walking, the head often made large rotations, usually in the yaw plane (up to 180°). The trunk, however, made only small pitch plane rotations (~10°). In contrast, during galloping, the head became fixed around earth-horizontal, with small rotations occurring only in the pitch plane (<20°). The trunk, however, experienced large pitch plane rotations (~40°). Thus, it appears that during slower gaits (walking), head rotations are not restricted because the trunk provides the spatial reference frame. During faster gaits (galloping) that require large angular displacements of the trunk, however, the head is restricted to provide the reference frame. Supported by the Amer. Inst. of Indian Studies, Nat. Geo. Soc. (USA), RCMI Award RR-03051 (NIH), and UPR Med. Sch. to D.C.D.

A-103 Suspensory Locomotion in *Lagothrix* and *Ateles*: Field and Controlled Observations of Positional Behavior. J.E. TURNQUIST, J.G.H. CANT, D. YOULATOS, Department of Anatomy, University of Puerto Rico, San Juan, PR; M.D. ROSE, New Jersey Medical School, Newark, NJ; D. SCHMITT, Duke University, Durham,NC.

Suspensory locomotion in two large prehensile-tailed New World monkeys, *Lagothrix* (woolly monkey) and *Ateles* (spider monkey), is superficially similar, yet detailed analysis shows significant differences in both frequencies of its use and its kinematics. Field studies in undisturbed forest in Yasuni National Park, Ecuador, provided quantitative observations, and videorecordings, of sympatric *Lagothrix lagothricha* and *Ateles belzebuth*. Forelimb swing and brachiation are two forms of suspensory locomotion utilized by both taxa. These two patterns of locomotion are similar in that they utilize forelimbs and tail but the former does not include trunkal rotation while the latter does. *Lagothrix* bouts of suspensory locomotion are shorter with a higher frequency of single steps and forelimb swings than *Ateles*. Triplanar videorecordings of captive *Lagothrix* and *Ateles* confirm the findings in the wild that *Lagothrix* suspensory locomotion is more conservative than that of *Ateles*. Frame by frame (1/30th of a second) analysis of suspensory locomotion reveals that taxa differ signficantly in the patterns of body movements during similar gaits. *Lagothrix* frequently utilizes a new tail hold with every hand hold (95%) while *Ateles* does not (28%), preferring to utilize a new tail hold with alternate hand holds. Suspensory locomotion in *Lagothrix* is thus very symetrical while in *Ateles* it is frequently asymetrical. The restraining force of the grasp of the prehensile tail limits free flight, and affects the length and velocity of the swinging pendulum as the body pivots under the hand hold during suspensory locomotion. This study shows how field data in combination with data from captivity provide a more meaningful picture of locomotor behavior than is possible with either alone. This work was supported by NSF Grant SBR-9222526, the UPR School of Medicine, and RCMI RR-03051 from NCRR, NIH.

A-104 **Prenatal Restraint Stress Effects on Locomotor Performance in Rats.** Wilfredo López[1], José Artecona[3], Sandra Morales[2], Carlos Mejias[4], Donald C. Dunbar[1], Benedikt Hallgrímsson[1], and Annabell C. Segarra[2]. University of Puerto Rico, [1]Dept. of Anatomy, [2]Dept. of Physiology, [1,2,3]School of Medicine, Medical Sciences Campus and [4]Dept.of Biology, Rio Piedras Campus.

We examined the effects of maternal restraint stress on the locomotor performance of Sprague-Dawley rats. Experimental dams were restraint stressed from gestation day 14-21, control dams were left understurbed. After birth, litters were culled to 10 pups/litter. At day 50, 30 males and 30 females were trained and subsequently tested for two endurance and two sub-maximal speed trials on a motor-driven treadmill. Females performed significantly better than males in both speed and endurance tests. Within each sex group, prenatally stressed individuals performed significantly less well on the speed tests. Our results thus suggest that prenatal restraint-stress does appear to adversely effect physiological performance as measured by locomotor performance on a treadmill. However, the magnitude of this stress-related effect is much smaller than sex-related differences in performance. Our results suggest that female rats may be adapted for higher levels of locomotor performance. This work was supported in part by an Institutional grant from the Deanship of Academic Affairs of the University of Puerto Rico, Medical Sciences Campus and by RCMI award RR-03051 from NIH.

A-105 Looking for Dihydroorotase Inhibitors Using Phage Display. SONIA M. ROBLES LOPEZ and BARBARA H. ZIMMERMANN. Department of Biochemistry, University of Puerto Rico, Medical Sciences Campus

Dihydroorotase (DHOase) is the third enzyme of the pyrimidine biosynthetic pathway, and catalyzes the cyclization of carbamyl aspartate to form dihydroorotate. During the reaction, a peptide bond is formed between the amino group of the carbamyl moiety and the carboxyl group side chain of the aspartate moiety. At low pH, the forward (biological) reaction is favored, while at high pH the reverse reaction is favored (Christopherson & Jones, 1979). Thus, under certain conditions, the DHOase acts like a protease. Furthermore, DHOase contains a zinc ion in its active site, as do many metalloproteases. We hypothesize that the DHOase, like proteases, may be inhibited by peptides. We will use a biopanning method to screen a random mixture of peptides displayed by phage. This method has succesfully been applied to screen for peptides which inhibit protease/substrate interactions. We have performed preliminary biotinylation experiments on a purified recombinant hamster DHOase to confirm that inactivation of the enzyme does not occur. The biotinylated DHOase will be immobilized on streptavidin-coated plates, and will be exposed to a library of phage displaying random peptides. Non-specifically bound phage are eluted, and E. coli are infected with the population of phage which bind more tightly. Several rounds of binding and amplification should yield a small group of peptides which will specifically interact with the DHOase. The peptides will be sequenced, and their inhibition will be confirmed using synthetic peptides. (Supported by RCMI Grant G12 RR 03051)

A-106 Hepatitis C Virus Genotype Prevalence and Interferon Treatment Outcomes in Puerto Rican Patients. J.R. RODRIGUEZ-MEDINA[1], W. PEREZ[1], J. GALLAGHER[2], J. MARTIN[3], F. CASTRO[3], AND E. TORRES[3]. Dept. of Biochemistry[1], UPR Med. Training Program[2], and Dept. of Medicine[3], Univ. of P.R., Sch. of Med.

Hepatitis C virus (HCV) is a positive strand RNA virus which is responsible for most cases of post transfusion non-A, non-B hepatitis. Significant patterns of RNA sequence variation have been described in the genome of this virus within the 5' UTR and within protein coding regions. A standardized nomenclature has been established to identify these variants. Recent studies by others have shown varying responses to treatment in patients infected with certain HCV sequence variants. Thus, monitoring of virus genotype should be included in the design and management of treatment protocols. We have performed analysis of HCV strain genotypes in patients currently on an interferon treatment protocol at the University Hospital Gastroenterology Clinic. The rationale for this analysis are 1) to identify the virus strain genotype infecting each patient and, 2) to establish if there is any correlation between the type of virus strain, mode of infection, disease progression, and treatment outcome. The method of analysis used was RT-PCR amplification of HCV RNA extracted from patient serum followed by Restriction Fragment Length Polymorphism analysis of these PCR products. To date we have screened 21 cases in which virus types 1b (12 cases), type 3a (1 case), and type 3b (8 cases) have been identified. Possible mixed infections have been detected in 3 cases. We have yet to determine any association between genotype and response to treatment. Supported in part by the UPR, School of Medicine and RCMI grants G12RR03051 and RCRII 1P20RR11126.

A-107 **First Steps in Continuous Quality Improvement of Hypertension Management**
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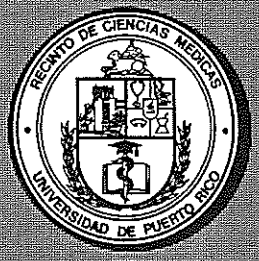
Background. The fist step in determining a cost-effective way to provide quality management of hypertension for a given population requires identification of factors not being adequately addressed but most likely to have a positive impact for the given population.

Methods. We administered questionnaires to patients, staff, and physicians, and performed chart reviews to collect information about the perceived barriers to effective treatment of hypertension. Student's t test and regression analysis were used to determine whether any correlation existed between degree of blood pressure control and cost and satisfaction, and also whether any correlation existed between cost and satisfaction.

Results. Blood pressure control as well as satisfaction was significantly less in African-American patients as compared to other patients. There was no significant correlation between blood pressure control and cost or satisfaction. There were no significant differences between smokers and non-smokers, or those who do not and who do exercise regularly, in blood pressure control, cost, or satisfaction. Physicians, staff and patients all perceived lifestyle modification as the greatest barrier to improvement. Cost of medications was also considered an obstacle.

Conclusions. Continuous quality improvement interventions in hypertension at our site may best focus first on facilitating patient changes in lifestyle and reducing the cost of medications. The patient population for whom the interventions are likely to have the greatest impact includes the African-American patients.



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