

# Trabajos enviados a congresos y/o Publicados en revistas internacionales durante el año 2002.

## **Anestesiología**

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*Biochim Biophys Acta 2002; 1562: 1-5*

A voltage-independent K<sup>+</sup> conductance activated by cell swelling in Ehrlich cells is modulated by a G-protein-mediated process.

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Cell swelling following hypoosmotic stress leads to the activation of volume-sensitive ion channels that allow a K<sup>+</sup> and Cl<sup>-</sup> efflux accompanied by water loss. A Ca<sup>2+</sup>-insensitive K<sup>+</sup> channel (I(K,vol)) has been described in Ehrlich cells that can be activated by hypotonicity and leukotriene D<sub>4</sub> and is inhibited by clofilium. We have studied the activation and deactivation by osmotic stimuli of this channel. A G-protein appears to be involved in these processes since GTP-γ-S accelerates deactivation, while GDP-β-S blocks the channel in the open state, a result mimicked by pertussis toxin (PTX). In addition, PTX accelerates the onset of I(K,vol). We propose that I(K,vol) is tonically inhibited by a PTX-sensitive G-protein.

*Biol Res 2002; 35: 215-22*

Non-selective cation channels and oxidative stress-induced cell swelling.

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Necrosis is considered as a non-specific form of cell death that induces tissue inflammation and is preceded by cell swelling. This increase in cell volume has been ascribed mainly to defective outward pumping of Na<sup>+</sup> caused by metabolic depletion and/or to increased Na<sup>+</sup> influx via membrane transporters. A specific mechanism of swelling and necrosis driven by the influx of Na<sup>+</sup> through nonselective cation channels has been recently proposed (Barros et al., 2001a). We have characterized further the properties of the nonselective cation channel (NSCC) in HTC cells. The NSCC shows a conductance of approximately 18 pS, is equally permeable to Na<sup>+</sup> and K<sup>+</sup>, impermeant to Ca<sup>2+</sup>, requires high intracellular Ca<sup>2+</sup> as well as low intracellular ATP for activation and is inhibited by flufenamic acid. Hydrogen peroxide induced a significant increase in cell volume that was dependent on external Na<sup>+</sup>. We propose that the NSCC, which is ubiquitous though largely inactive in healthy cells, becomes activated under severe oxidative stress. The

ensuing Na<sup>+</sup> influx initiates via positive feedback a series of metabolic and electrolytic disturbances, resulting in cell death by necrosis.

## **Cardiovascular**

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*Cardiovasc Surg 2002; 10: 264-75*

### **Carney's syndrome: complex myxomas. Report of four cases and review of the literature.**

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Cardiac myxomas are rare tumors. They usually appear as a sporadic isolated condition in the left atrium of middle-aged women with no other coincidental pathology. Carney and others have described in young people a special complex group of cardiac myxomas associated to a distinctive complex pathology, giving identity to the "Syndrome Myxoma" or "Carney's Syndrome". Four additional cases of this syndrome, treated from 1977 to 1999 at the Hospital Clínico de la Universidad de Chile are presented here with a comprehensive review of the literature, accumulating 100 cases. The main features of our cases include the presence of malignant non cardiac tumors, a familial trend, follow-up of 23 years and an iterative recurrence in the elder case. To date all patients are tumor free. Reviewing the literature, patients with Carney's Syndrome were younger, with a mean age of 26 years and female predominance (62%). Cardiac myxomas affected the four chambers of the heart: 64% the left atrium; 44% the right atrium; 14% the left ventricle and 12% the right ventricle. They were multiple tumors in

41% and involved more than one chamber in 31%, being synchronous or metachronous. There was a marked familial trend (52%), a high incidence of recurrence (20%), with more than one occurring in half the cases. Extra-cardiac involvement consisted of: 68% pigmented skin lesions, 40% cutaneous myxomas, 37% adrenal cortical disease, 27% myxoid mammary fibroadenoma and 34% male patients with testes tumors. A low percentage had pituitary adenoma, melanotic schwannomas and thyroid disease. The diagnosis is made when two or more of these criteria are present. In agreement with these findings the four chambers of the heart should be examined at surgery for atypical myxoma locations, right atriotomy and combined superior-transseptal approach improve exposure of the cavities, careful screening of the first degree family members should be conducted, and closed short and long term follow up controls are important. Complex myxoma appears as a multi-systemic disorder, occasionally having an ominous prognosis and malignant potentiality, and is still undergoing investigation for better understanding and identification.

Esperamos diseñar un instrumento de medición del impacto de tales reuniones en relación con la mejora de los procesos internos y la satisfacción usuaria.

## **Cirugía**

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World J Surg 2002; 26: 1228-33

### **Barrett's esophagus complicated with stricture: correlation between classification and the results of the different therapeutic options.**

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Benign esophageal stricture is a serious complication of persistent gastroesophageal reflux in patients with esophagitis and Barrett's esophagus. A classification of the severity of the stricture is proposed, based on its internal diameter, its length, and the ease or difficulty in dilating it. Among 185 patients with esophageal strictures secondary to reflux esophagitis, 77 (41.6%) corresponded to type I or mild stricture, 73 (39.4%) to type II or moderate, and 35 (19.6%) to type III. Medical treatment was performed in only 15 cases, with 73% recurrence. Three types of surgical procedures were employed, always after dilatation, improvement of nutritional status, and a complete preoperative work-up: (1) conservative antireflux surgery, which had a high incidence of recurrence (41.1%); (2) acid suppression and duodenal diversion, in which 68 patients had a mortality rate of 2.9% and a recurrence rate of 4.4% ( $p < 0.002$ ); and (3) esophageal resection, which in 7 patients resulted in 1 death and no late recurrence. It is concluded that classifica-

tion of the severity of the stricture is important to indicate the most appropriate treatment. Conservative antireflux surgery is followed by a high recurrence rate at late follow-up, whereas acid suppression and duodenal diversion seem to be an adequate procedure that is followed by a very low recurrence rate. Esophageal resection is indicated only for patients with severe or critical esophageal strictures.

*Dis Esophagus 2002; 15: 315-22*

## Results of surgical treatment for recurrent postoperative gastroesophageal reflux.

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The rate of recurrence of reflux esophagitis after classic antireflux surgery (fundoplication) is 10-15%. This rate is different in patients with esophagitis with and without Barrett's esophagus. We evaluated the clinical and laboratory findings in 104 patients with postoperative recurrent reflux esophagitis, determining the results of repeat antireflux surgery or an acid suppression-bile diversion procedure. Repeat fundoplication was performed in 26 patients, and truncal vagotomy, antrectomy, and Roux-en-Y gastrojejunostomy in 78 patients. Esophagectomy as a third operation was performed in seven patients. After repeat antireflux surgery, endoscopic evaluation demonstrated improvement of esophagitis in a small proportion of patients. Barrett's esophagus remained unchanged, and no regression of ulcer or stricture was observed. These complications

improved significantly after acid suppression-bile diversion surgery. Incompetent lower esophageal sphincter (LES) was present in 55.8% after initial surgery and in 23% after reoperation. Acid reflux, initially present in 94.6% of patients, was also observed in 93.6% after fundoplication, 68.8% after redo fundoplication, and 16.6% after treatment with the acid suppression-bile diversion technique. A positive Bilitec test was present in 78% of patients before the operation and 56.6% after the repeat operation, and was negative after bile diversion surgery. Among 13 patients (50%) submitted to repeat surgery alone, esophagectomy as a third operation was necessary as a result of severe non-dilatable stricture in seven patients. Our conclusions are that repeat antireflux surgery alone failed to improve Barrett's esophagus complications and that the best results were obtained in patients submitted to acid suppression-bile diversion surgery.

## Dysplasia and adenocarcinoma after classic antireflux surgery in patients with Barrett's esophagus: the need for long-term subjective and objective follow-up.

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**Objective:** To assess the clinical, endoscopic, and functional results in a group of patients with Barrett's esophagus undergoing classic antireflux surgery in whom dysplasia and adenocarcinoma were found at a late objective follow-up. **Summary background data:** There have been isolated reports of patients with Barrett's esophagus undergoing antireflux surgery who show dysplasia or even adenocarcinoma on follow-up. **METHODS:** Of 161 patients undergoing surgery, dysplasia developed in 17 (10.5%) at late follow-up and adenocarcinoma developed in 4 (2.5%). These 21 patients represent the group assessed and were compared with 126 surgical patients with long-segment Barrett's in whom dysplasia did not develop. They were evaluated by clinical questionnaire, multiple endoscopic procedures and biopsy specimens, 24-hour pH studies, and 24-hour bilirubin monitoring. **Results:** Of the 17 patients with dysplasia, 3 were asymptomatic at the time that dysplastic changes appeared; all patients with adenocarcinoma had symptoms. Two patients (12%) in the dysplasia group had short-segment Barrett's; all patients with adenocarcinoma

had long-segment Barrett's. Manometric studies revealed an incompetent lower esophageal sphincter in 70% of the dysplasia group, similar to nondysplasia patients with recurrence, and in 100% of the adenocarcinoma group. The 24-hour pH study showed pathologic acid reflux in 94% of the patients with dysplasia, similar to patients with recurrence without dysplasia, whereas bilirubin monitoring showed duodenal abnormal reflux in 86% of the patients. Among patients with dysplasia, three different histologic patterns were identified. All patients with adenocarcinoma had initially intestinal metaplasia, with appearance of this tumor 6 to 8 years after surgery. **CONCLUSIONS:** Patients with Barrett's esophagus who undergo antireflux surgery need close and long-term endoscopic and histologic surveillance because dysplasia or even adenocarcinoma can appear at late follow-up. Metaplastic changes from fundic to cardiac mucosa and then to intestinal metaplasia and later to dysplasia or adenocarcinoma can clearly be documented. There were no significant differences in terms of clinical, endoscopic, manometric, 24-hour pH, and bilirubin monitoring studies between patients with recurrence of symptoms without dysplastic changes, and patients with dysplasia. Therefore, the high-risk group for the development of dysplasia is mainly the group with failed antireflux surgery.

## Early and late results of the acid suppression and duodenal diversion operation in patients with Barrett's esophagus: analysis of 210 cases.

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The usual surgical treatment for patients with Barrett's esophagus (BE) is a classic Nissen fundoplication or posterior gastropexy with cardial calibration. However, some surgical reports as well as our experience suggest that the rate of failure of the Nissen fundoplication or Hill's posterior gastropexy in patients with BE is significantly higher than in those with reflux esophagitis without BE, probably due in part to the persistence of duodenal reflux into the esophagus. Our aim was to determine the late subjective and objective results of an operation consisting in «acid suppression» (vagotomy-partial gastrectomy) and «duodenal diversion» (Roux-en-Y anastomosis) as a primary surgical procedure for patients with BE. Altogether, 210 patients were subjected to this technique. It consisted in a primary operation in 142 patients and revision surgery in 68. They underwent complete clinical, radiologic, endoscopic, histologic, and manometric studies. In some cases 24-hour pH studies, Bilitec studies, gastric emptying, and gastric acid secretion evaluations were performed. There were two deaths (0.95%), and postoperative morbidity was low (5.3%). The late mean follow-up (58 months) for 146 patients who completed a

follow-up longer than 24 months showed Visick I and II grades in 91.1% of the cases. In 14.9% of the cases 24-hour pH monitoring showed excessive acid reflux 1 year after surgery. No dysplasia or adenocarcinoma has appeared up to now. Functional studies showed significant alleviation of lower esophageal sphincter (LES) incompetence, with abolition of duodenal reflux into the esophagus. Gastric emptying of solids was normal, and basal and peak gastric acid output remained at a low level 8 to 10 years after surgery. In patients with BE, with severe damage of the LES and esophageal peristalsis, the «suppression diversion» operation completely abolishes the reflux of injurious components of the refluxate and improves sphincter competence. This effect is permanent and avoids the appearance of dysplasia or adenocarcinoma.

*Chest Surg Clin N Am 2002; 12: 157-84*

## Roux-en-Y long limb diversion as the first option for patients who have Barrett's esophagus.

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In summary, vagotomy plus antrectomy and the Roux-en-Y procedure is based on the following points: (a) patients who have BE show several foregut abnormalities, including incompetent lower esophageal sphincter, impairment in the esophageal clearance, severe gastroesophageal acid reflux, and frequent duodeno-esophageal reflux; (b) late results of classic antireflux procedure in BE are poor with a high recurrence rate owing to a

progressive loosening of the wrap; (c) the esophageal damage is produced by the injurious component of the refluxate; and (d) among patients who underwent classic antireflux surgery, a certain proportion developed dysplasia or even adenocarcinoma in the follow-up. The authors have observed that the simple correction of the valve is not enough in many cases, because it does not abolish the gastroesophageal reflux but only diminishes it. In patients who have BE and therefore have impaired esophageal clearance, few reflux episodes can maintain or even induce more damage. With the reduction diversion antireflux procedure, the quality of the corrected valve is secondary, and the main goal is to avoid the reflux of injurious components of the refluxate instead of the refluxate itself, which is almost always impossible. Late results support this hypothesis, and the authors propose this surgical procedure as an alternative treatment in patients who have complicated BE or in patients who have long-segment BE. Among patients who have gastroesophageal reflux and intestinal metaplasia of the cardia or with a noncomplicated short-segment BE, laparoscopic antireflux surgery is the authors' first choice, and only the late objective evaluation of surgical treatment demonstrates which surgical technique is the more adequate to a particular patient who has BE.

*Surgery 2002; 131: 401-7*

## A prospective randomized study comparing D2 total gastrectomy versus D2 total gastrectomy plus splenectomy in 187 patients with gastric carcinoma.

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**Background:** Classic surgical treatment of upper third gastric carcinoma is based on an extended total gastrectomy, including splenectomy. The purpose of this study was to perform a prospective randomized clinical trial comparing the early and late results of total gastrectomy (TG) versus total gastrectomy plus splenectomy (TGS). **METHODS:** One hundred eighty-seven patients with gastric carcinoma were included. In all patients a D2 total gastrectomy was performed. During surgery they were randomized to 1 of 2 operative options. They were monitored to their death or to 5 years later if they were alive. **RESULTS:** Operative mortality was similar after both operations (3% after TG and 4% after TGS). Septic complications after surgery were higher after TGS compared with TG ( $P < .04$ ). Five-year survival rates were not statistically different between groups or in subset analysis according to stage of disease. **CONCLUSIONS:** On the basis of the results of the present prospective randomized trial, splenectomy is not necessary in early stages of disease. A low operative mortality rate (less than 3%) must be achieved to obtain good long-term results.

## Clinical, endoscopic, and functional studies in 408 patients with Barrett's esophagus, compared to 174 cases of intestinal metaplasia of the cardia.

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**Objective:** The pathophysiology of gastroesophageal reflux disease (GERD) has been studied extensively in patients with long-segment Barrett's esophagus (LSBE), but few reports have explored GERD pathophysiology in patients who have short-segment Barrett's esophagus (SSBE) or intestinal metaplasia at the cardia (IMC). We aimed to compare clinical, endoscopic, histological, and functional features in patients with LSBE, SSBE, and IMC. **METHODS:** We identified 582 patients who had intestinal metaplasia at the squamocolumnar junction in the distal esophagus and divided them into three groups based on the extent of columnar-lined esophagus observed endoscopically: 1) patients with IMC who had no columnar-lined esophagus (i.e., the squamocolumnar and gastroesophageal junctions coincided), 2) patients with LSBE who had >3 cm of columnar-lined esophagus, and 3) patients with SSBE who had <3 cm of columnar-lined esophagus. All patients had esophageal manometric evaluation, and 24-h esophageal pH monitoring was performed to determine the extent of acid and bile

(bilirubin) reflux. **Results:** There were 174 patients with IMC, 155 with LSBE, and 25 with SSBE. Compared to patients with LSBE and SSBE, patients with IMC had significantly lower frequencies of GERD symptoms, hiatal hernia, and erosive esophagitis; significantly higher lower esophageal sphincter pressures; and significantly shorter durations of acid and bile reflux. Between patients with SSBE and LSBE, significant differences were found in the frequency of hiatal hernia and duration of acid reflux (both greater in the patients with LSBE). Also, dysplasia was significantly more frequent in patients with LSBE than in those with SSBE or IMC. **CONCLUSION:** GERD symptoms, signs, and physiological abnormalities are found more often in patients with Barrett's esophagus than in those with IMC, and the duration of acid reflux in patients with LSBE is greater than that in patients with SSBE. These findings suggest that the extent of intestinal metaplasia in the esophagus is related directly to the severity of underlying GERD.



## Effect of duodenal diversion on low-grade dysplasia in patients with Barrett's esophagus: analysis of 37 patients.

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It is well known that in patients with Barrett's esophagus (BE), even after antireflux surgery, intestinal metaplasia can progress to dysplasia or even adenocarcinoma. However, the opposite—that is regression of dysplastic changes to intestinal metaplasia after antireflux surgery—has been documented in only a few reports. The objective of this study was to determine the effect of a duodenal diversion operation on low-grade dysplasia in patients with BE. Thirty-seven patients with either short-segment ( $n = 12$ ) or long-segment ( $n = 25$ ) BE underwent antireflux surgery plus either a duodenal switch procedure (13 patients) or a partial distal gastrectomy with Roux-en-Y gastrojejunal anastomosis (24 patients). All of them were subjected to complete clinical, endoscopic, histologic, manometric, and 24-hour pH testing, and 24-hour monitoring of the bile exposure in distal esophagus. There were no deaths in this series, and morbidity occurred in only one patient (2.7%). Manometric assessment after surgery showed a significant increase in sphincter pressure, abdominal length, and total length ( $P < 0.001$ ). Acid reflux showed a significant decrease after surgery, and duodenal reflux was completely abolished in all except one patient. Follow-up in all patients was longer than 24 months (mean 60 months). Three to

four endoscopic procedures were performed after surgery in each patient, and several biopsy specimens were taken distal to the squamo-columnar junction during each endoscopic procedure. Eleven patients (91%) with short-segment BE demonstrated histologic regression to either cardiac mucosa or nondysplastic intestinal metaplasia. Among the 25 patients with long-segment BE, there was a 62.5% rate of histologic regression to nondysplastic epithelium when the length of BE measured between 31 and 99 mm and 33% histologic regression when the length of BE was 101 mm or more. There were no cases of progression to high-grade dysplasia or adenocarcinoma. The endoscopic length of the columnar-lined esophagus did not change late after surgery. In 65% of patients with BE, antireflux surgery, gastric acid reduction, and duodenal diversion produced histologic regression of low-grade dysplasia to nondysplastic mucosa. This effect was even more pronounced when the length of BE was shorter. It seems to be permanent, and no progression to high-grade dysplasia or adenocarcinoma has occurred.

## Dentomáxilofacial

*Biological Research 2002; 35: R-48*

Efectos de la domesticación en *Cavia porcellus* sobre la variación de la forma del cráneo: análisis de la morfometría lineal y geométrica (Effects of domestication on the skull shape variation of *C. porcellus*: a lineal and geometric morphometric analysis)

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Antecedentes y Problemas: Las cepas de *C. porcellus* (andinas y europeas o de laboratorio), eventualmente se originaron a partir de un evento único de domesticación en los Andes centrales, y tuvieron como especie hipotética ancestral a *C. tschudii*. No se conocen las consecuencias biológicas de este proceso.

Hipótesis: Aumento progresivo del síndrome de domesticación (variación neoténica de la forma calvaria) en la dirección (*C. tschudii*, N= 19) (*porcellus* Andino (N=28) (*porcellus* europeo (N=23).

Resultados y conclusión: El análisis de las curvas de crecimiento log/log de ambas cepas de *porcellus* mostró diferencias significativas

en la variación de la forma total sensu Bookstein (distintos valores del intercepto a iguales pendientes, ANCOVA). El análisis de morfometría geométrica para 21 hitos anatómicos en vista lateral (relative warp analysis) mostró la contracción de los vectores calvarios del neurocráneo de las cepas europeas de *porcellus* en comparación a la cepa andina ya la especie silvestre *C. tschudii*. Estos resultados sugieren que uno de los efectos de la domesticación del cuy es la neotenzación de la forma del cráneo en la dirección *tschudii* - *porcellus* andino - *porcellus* europeo.

Proyecto Fondecyt N°1011052

*Biological Research 2002; 35: R-61*

Polimorfismo -308 del promotor del factor de necrosis tumoral y expresión de TNF inducida por la lopolisacarido en pacientes con periodontitis agresiva y/o Diabetes Mellitus tipo 1

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Las periodontitis son respuestas inmuno-inflamatoria, mediadas por citoquinas tales como TNF, siendo la Diabetes Mellitus (DM) un factor de riesgo Se estudió la asociación del polimorfismo mononucleotídico (SNP) -308 de TNF

con la susceptibilidad a periodontitis agresiva (PA). PA asociada a dm1 (PAADM1), y DM1. Analizamos también la relación entre el SNP-308 y la expresión de TNF. Se reclutaron 20 individuos PAADM1, 21 DM1, 18 PA y 19 controles. El alelo TNF2 estuvo presente en el 17% de PA, 35% en PAADM1, 5% en DM1 y 16% en controles. El odds ratio (2.87) sugiere una asociación entre el SNP-308 y PAADM1, aunque no fue estadísticamente significativa ( $p=0.17$ ). El TNF inducido por LPS fue mayor en PA y PAADM1 en comparación con los controles ( $p=0.0002$  y  $0.0414$  respectivamente). Las concentraciones séricas en todos los grupos fueron 3 veces mayor que el grupo control. No se encontró asociación entre el SNP-308 y los niveles de TNF séricos y ex vivos en PA, PAADM1 y DM1. Financiamiento FONDECYT 19909.16.DID-ENL-02-13.

## **Dermatología**

*XVI Reunión Anual de Dermatólogos Latinoamericanos del Cono Sur (RADLA), 4-7 mayo (2002, Santa Cruz, Bolivia)*

### **Pitiriasis Rosada de Gilbert: Prevalencia en población consultante**

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La Pitiriasis Rosada (PR) es una erupción cutánea pápuloescamosa que se caracteriza por la aparición de una lesión inicial o placa heráldica, que después de una o dos semanas es seguida por una erupción secundaria generalizada, que dura alrededor de seis semanas. Existen pocos estudios en la literatura mundial que informen sobre la prevalencia e incidencia de esta enfermedad. En Chile no se han realizado estudios de prevalencia de PR, ni su relación con el sexo, la edad o estación del año en que se presenta. Por esta razón hemos realizado este estudio que tiene por objetivo estimar la prevalencia PR en población consultante a un servicio de Dermatología hospitalario y describir el comportamiento de esta enfermedad en relación a estas variables. Se revisó el total de las fichas clínicas de los pacientes que consultaron al Servicio de Dermatología del Hospital Clínico de la Universidad de Chile durante el año 1999. Se apartaron las fichas en que el médico dermatólogo diagnóstico clínicamente PR y se consignó sexo edad del paciente y fecha en que la consulta fue realizada. Se construyó una base de datos con los resultados y éstos se analizaron con el programa es-

estadístico EpiInfo 6.04. Los resultados obtenidos fueron los siguientes: Durante 1999 se realizaron 12.700 consultas al servicio de Dermatología del Hospital Clínico de la Universidad de Chile. De éstas el 0,38% fueron catalogadas como PR, con una razón hombre/mujer de 0,26 y una media edad de 25 años, con un rango que va desde los 4 a 47 años. El mes del año con más consultas por esta enfermedad fue Mayo con un 14,6% del total de PR y la estación del año que presenta mayor número de pacientes es el Otoño.

La prevalencia anual de PR en la población consultante al Servicio de Dermatología del Hospital Clínico de la Universidad de Chile es semejante a lo encontrado en la literatura mundial, afectando en una mayor proporción a las mujeres y al grupo de adultos. Al igual que en muchos reportes mundiales, esta enfermedad se presentó con mayor frecuencia en los meses fríos del año.

Es el primer estudio de prevalencia de esta enfermedad realizado en nuestro medio, lo que permite la planificación de otros trabajos destinados a encontrar la etiología de la PR y probables tratamientos.

*RADLA 2002, Santa Cruz, Bolivia*

## Tasas de Incidencia de cáncer cutáneo en Santiago, Chile y su distribución por grupo etáreo en el período 1992 - 1998.

Tipo de Presentación: Trabajo de Investigación, Sección.

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Durante la última década se ha registrado un incremento de la incidencia de cáncer cutáneo a nivel mundial. El objetivo de este trabajo fue el de determinar las tasas de incidencia de cáncer cutáneo en la población beneficiaria de Santiago en el período 1992 - 1998 e identificar grupos etáreos de riesgo dentro de la población estudiada. Para este objetivo, se analizaron aproximadamente 350.000 informes histopatológicos de hospitales públicos de Santiago, que cubren una población aproximada de dos millones de habitantes. Se obtuvieron las poblaciones asignadas de cada hospital/año y se calcularon las tasas de incidencia totales y de cada tumor cutáneo. En relación a la distribución por grupo etáreo, se dividió la población en pacientes a) < 40 años, b) entre 40 - 60 años, c) > 60 años. Se estudió el % total de tumores, el % de cada tumor y la agresividad histológica / año en cada uno de estos grupos etáreos. En nuestro estudio, las tasas de incidencia totales de cáncer cutáneo aumentaron un 43% entre 1992 y 1998. Las tasas de incidencia de Melanoma Maligno (MM) aumentaron un

105%, de Carcinoma Espino Celular (CEC) aumentaron un 86% y de Carcinoma Basocelular (CBC) aumentaron un 26%.

Con respecto a la distribución por edad, un 75% de los tumores totales estudiados se encontraba en el grupo de > 60 años, un 20% de los tumores se ubicaba en el grupo 40 - 60 años y solamente un 5% en el grupo < 40 años. Con respecto al MM, un 58% de los tumores se encontraba en el grupo > 60 años, en cambio en el CEC un 82% y en el CBC un 76%. Con respecto a la agresividad histológica de los tumores, en el MM y en el CEC, en los distintos grupos de edad, no se observan cambios significativos en el período estudiado, en cambio en el CBC, se observa un aumento significativo de tumores agresivos en el grupo > 60 años en el período 1992 - 1998. En este estudio, a pesar de que se obtuvieron tasas de incidencia de cáncer cutáneo inferiores a las informadas en la literatura internacional, realizadas en población caucásica, es preocupante el aumento de las tasas, tanto en el total de tumores, como en cada tumor en el período 1992 - 1998. La gran mayoría de los tumores cutáneos estudiados se encontraba en el grupo de mayor edad (> 60 años), esto coincide con la literatura internacional con respecto al CBC y al CEC, sin embargo en el MM, nuestros casos son de mayor edad que los informados en la literatura internacional. Este estudio presenta resultados preliminares en relación a la incidencia de cáncer cutáneo en Chile.

*American Association of Dermatologists February 22-27, 2002. New Orleans, LA.*

## Pattern of distribution of the peritumoral infiltrate associated to basal cell carcinoma.

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60th Annual Meeting of the American Academy of Dermatology

**Introduction:** Basal Cell Carcinoma (BCC) is the most common malignancy in humans. The identification of the BCC's peritumoral infiltrate has been mainly characterized by the use of the immunohistochemistry technique. Those studies have been performed in selected peritumoral, interfollicular areas without looking at the total inflammatory infiltrate's distribution in the all tissue. The purpose of this study was to look at the peritumoral distribution of the inflammatory infiltrate in BCC in the all tissue, with the idea of identifying a common pattern of distribution.

**Methodology:** Immunohistochemical staining with anti CD45, anti CD25 and anti CD56 monoclonal antibodies was performed in frozen sections of IO facial BCC (5 males, 5 females), 100% solid or predominantly solid histologically, who ranged in aged from 49 yrs. to 84 yrs.

Positive cells were counted with the help of an ocular grid, as percentages of the total cell infiltrate per unit of area in two well defined regions surrounding the tumour, region A: immediately close to the tumour and region B: 430 um. far from the tumour. Non parametric Wilcoxon test was used for the statistical analysis. **Results:** 74% of the total infiltrate was CD45 + (inflammatory cells).

Regarding the distribution of these inflammatory cells, we found a significant higher number of CD45+ cells in the region A than in region, B (  $p < 0.05$ ). Also, we found inflammatory cells at the tumour border in the majority of the samples and also it was interesting to observe a high number of these cells to be present around hair follicles. 12% of the total infiltrate was CD 25+ (activated T cells). 0.77% of the infiltrate was CD56+ (natural killer cells). Interestingly, this antibody shows a special affinity to dendritic cells in superficial dermis and perifollicular areas:

Conclusions: The study of the distribution of inflammatory cells in the all of the peritumoral area allow as to draw a picture of a pattern of distribution of the inflammatory infiltrate in BCC. This pattern was very much the same in the all tumours studied. This pattern of distribution with a higher inflammatory cells around the tumour and around hair follicles may be associated with a biological, clinical behaviour of the tumour .

*RADLA 2002, Santa Cruz, Bolivia.*

## Dermatomiositis diagnosticadas en el Hospital Clínico Universidad de Chile y asociación con neoplasia

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La Dermatomiositis es una enfermedad de etiología desconocida que se presenta con una erupción cutánea característica, la cual se puede manifestar con o sin miopatía proximal. Se trata de una patología de baja incidencia en la consulta dermatológica, sin embargo, durante el año 2001 se observó un aumento de la incidencia de casos de Dermatomiositis diagnosticados en el Servicio de Dermatología del Hospital Clínico de la Universidad de Chile. Por este motivo se decide presentar 5 de los casos más estudiados, destacando en dos de ellos su asociación con neoplasia (cáncer de páncreas y adenocarcinoma mamario oculto).

## Carcinoma espinocelular en Región Metropolitana Chile: Incidencia y características epidemiológicas (1992 a 1998)

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El carcinoma espinocelular (CEC), es una neoplasia maligna, de etiología multifactorial. Existe amplio consenso internacional del aumento en la incidencia del CEC en los últimos años, que cobra mayor relevancia por su rápido crecimiento y riesgo de metástasis. En la actualidad es considerado como un problema de salud. En Chile existen escasos estudios epidemiológicos del CEC. Objetivos: Determinar la incidencia del CEC y sus probables factores de riesgo. Analizar las variables epidemiológicas de los pacientes con CEC y su tendencia a lo largo del estudio; en población chilena. Pacientes y métodos: De un total de 330.000 informes histopatológicos revisados, entre Enero de 1992 a Diciembre de 1998, en 5 hospitales públicos de la Región Metropolitana; se relacionaron las informadas como CEC (n=°78). Resultados: representa el 27% de todos los cánceres de piel. Su incidencia aumentó de 3,7 a 6,8 por 100.000 habitantes, entre 1992 y 1998. La prevalencia fue de 52,6 por 100.000 habitantes, 568 eran hombres y 410 mujeres (p<0,001). El promedio de edad fue de 70+14,5 años (rango 15 a 98), más frecuente en > de 65 años

(61,5%). La localización más frecuente fue en zonas fotoexpuestas 61% (p<0,0001). El mayor grado de indiferenciación se encuentra en hombres y en mayores de 65 años. Conclusiones: En nuestra población el CEC es el segundo cáncer de piel más frecuente. Se evidenció un aumento progresivo y significativo en su incidencia y el riesgo de CEC aumentó en 1,8 veces entre 1992 y 1998. Los factores de riesgo identificados en nuestros estudios son: sexo masculino, edad avanzada y fotoexposición.

*Int J Dermatol 2002; 41: 99-103*

## Malignant melanoma mortality rates in Chile (1988-98).

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Background: Malignant melanoma (MM) mortality has increased in the Caucasian population many fold over the past several decades. In this study, we analyzed the Chilean-specific, age-adjusted MM mortality rates per 100,000 population during the decade 1988-98 in order to establish changes in that period. METHODS: We analyzed all death certificates from the Chilean Death Registry Office (1988-98) and retrieved the deaths attributed to MM. The data were categorized according to sex and age group. The annual age-adjusted and sex-specific rates of MM mortality per 100,000 population were calculated. RESULTS: Chilean MM mortality rates increased by 14% between 1988 and 1998. The relative risk for males vs. females was 1.3 with a tendency to rise, showing an increase of 30%. The relative risk of dying from

MM in Chile increased linearly with age. An individual of 75 years or older had a 44.24 times greater risk of dying of MM than an individual in the 0-44-year age group. The rates in the > 75-year age group also showed a tendency to rise over the decade, with an increase of 64% (1988-98). CONCLUSIONS: The Chilean MM mortality rates are lower than the world standardized rates. The total Chilean MM mortality rates showed an increase over the decade 1988-98, mainly due to MM mortality in males. The MM mortality in Chilean females was lower than that in males, and was unchanged over the decade; this is in agreement with the results reported in other countries. This is one of the first studies of MM mortality in the Chilean population. The results are important when the geographic location of Chile is considered.

## **Endocrinología**

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*Eur Cytokine Netw 2002; 13: 419-24*

### **Evaluation of tumor necrosis factor alpha production in ex vivo short term culture whole blood from women with polycystic ovary syndrome.**

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In mammals, the pleiotropic biological functions of tumor necrosis factor alpha (TNF- $\alpha$ ) may include important effects on human reproductive physiology. Thus, chronic anovulation, oligo or amenorrhea, infertility, hyperandrogenism, obesity, insulin resistance and increased TNF $\alpha$  serum levels have been observed in women affected by polycystic ovary syndrome (PCOS). Whole blood short-term cell cultures (WBSC) are simple systems where the capacity to produce TNF- $\alpha$  by circulating leukocytes, mainly of the macrophage/monocyte lineage, can be accurately quantified. Given the relevance of monocytes/macrophages in the production of TNF- $\alpha$ , in this study, in a control-case approach, WBSC from women with PCOS were analyzed in their basal and lipopolysaccharide (LPS)-stimulated capacity to produce the cytokine. These measurements did not correlate with the increased serum levels of the cytokine and the normal levels of cortisol, found in PCOS women. Increased serum TNF- $\alpha$  levels in PCOS women correlated positively with body



mass index and negatively with insulin sensitivity. In spite of the increased serum TNF- $\alpha$  levels in PCOS women, basal and LPS stimulated production of the cytokine, by the ex vivo WBSC from these patients, were within normal values.

*Microsc Res Tech* 2002; 59: 509-15

## Neurotrophic control of ovarian development.

Dissen GA, Romero C, Paredes A, Ojeda SR.

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Substantial evidence now exists indicating that the neurotrophins, a family of growth factors required for the survival, development, and differentiation of various neuronal populations of the nervous system, are also important for the development of nonneuronal tissues. Such a function was first suggested by studies showing the presence of high-affinity neurotrophin receptors in a variety of nonneuronal tissues including those of the cardiovascular, endocrine, immune, and reproductive systems. Within the latter, the gonads appear to be a preferential site of neurotrophin action as suggested by the presence in the mammalian ovary of at least four of the five known neurotrophins and all of the neurotrophin receptors thus far identified. While the various functions that the neurotrophins may have in the ovary are still being elucidated, it is now clear that in addition to recruiting the ovarian innervation, they play a direct role in the regulation of two different maturational periods that are critical for the acquisition of female reproductive function: early follicular development and ovulation. Neurotrophins facilitate the development of

newly formed follicles by promoting the initial differentiation and the subsequent growth of primordial follicles. These actions appear to be related to the ability of neurotrophins to sustain the proliferation of both mesenchymal and granulosa cells, and to induce the synthesis of follicle stimulating hormone (FSH) receptors. At the time of the first ovulation, neurotrophins contribute to the ovulatory cascade by increasing prostaglandin E(2) release, reducing gap junction communication, and inducing cell proliferation within the thecal compartment of preovulatory follicles. *Microsc. Res. Tech.* 59:509-515, 2002. Copyright 2002 Wiley-Liss, Inc.

*Endocrinology* 2002; 143: 1485-94

## Nerve growth factor induces the expression of functional FSH receptors in newly formed follicles of the rat ovary.

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The neurotrophin nerve growth factor (NGF) and its two membrane-anchored receptors are expressed in the developing ovary before the organization of the first primordial follicles. In the absence of NGF, the growth of primordial follicles is retarded, indicating that NGF contributes to facilitating early follicular development. The present experiments were undertaken to determine whether NGF can also be involved in the differentiation process

by which ovarian follicles become responsive to gonadotropins. Treatment of 2-d-old rat ovaries in organ culture with NGF increased FSH receptor (FSHR) mRNA within 8 h of exposure. This effect was cAMP-independent but additive to the cAMP-mediated increase in FSHR gene expression induced by either forskolin or vasoactive intestinal peptide, a neurotransmitter previously shown to induce FSHR formation in neonatal rat ovaries. After NGF treatment, the ovary acquired the capacity of responding to FSH with cAMP formation and preantral follicular growth, indicating that exposure to the neurotrophin resulted in the formation of biologically active FSHRs. Quantitative measurement of FSHR mRNA demonstrated that the content of FSHR mRNA is reduced in the ovaries of mice carrying a null mutation of the NGF gene. These results indicate that one of the functions of NGF in the developing ovary is to facilitate the differentiation process by which early growing follicles become gonadotropin-dependent during postnatal life, and that it does so by increasing the synthesis of FSHRs.

## **Gastroenterología**

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*XVII Congreso Asociación Latinoamericana para el estudio de el hígado (ALEH)*

*Gastroenterol Hepatol 2002; 25: (S2) 13*

### **Peg-interferón en Riba Virina en Hepatitis Crónica C. Informe preliminar.**

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Introducción: El PEG-Interferón (PI) ha demostrado mayor Comodidad de administración y mejor efecto antiviral que el interferon "clásico" en pacientes con hepatitis crónica C (HCC). Su uso en combinación con Ribavirina (RV) por 24-48 semanas es el tratamiento de elección en la actualidad en estos casos, sin que exista información al respecto en nuestro medio. Objetivo: Conocer el efecto de la terapia combinada con PI y RV en HCC.

Pacientes y métodos: Entre VII/O1 y III/O2 veinte casos con HCC con confirmación histológica y viremia positiva (12 hombres, edad  $x 46 + 9$  años), fueron protocolizados para recibir PI (PEGASYS Lab. Roche) 180 ug/semana y RV 800 mg/día por 48 semanas. Se controlaron periódicamente con hemograma y pruebas hepáticas y carga viral a las 24 y 48 semanas de tratamiento y se controlarán a las 24 semanas de su término.

Resultados: 15 casos tenían solo hepatitis crónica y 4 además cirrosis (1 hemofílico no biopsiado), 17 tenían genotipo 1b y 3 casos 3a. Hasta VIII/O2. solo 10 pacientes han completado 48 semanas de tratamiento, obteniéndose los siguientes resultados:

Semana	n	Viremia (+)	Hb x	Neutr. X	Plaqa. X	SGOT x	SGTP x
Basal	20	20	15,3	3121	197.050	115	176
8	20	-	12,6	1610	138.650	62	76
24	17	3	12,3	1518	134.741	69	86

La terapia ha sido bien tolerada, aunque 7 pacientes presentaron prurito y/o dermatitis y 1 poliartritis seronegativa autolimitada. La dosis de PI debió reducirse por neutropenia en sólo 1 caso y la RV por anemia en 4 casos, debiendo suspenderse transitoriamente en 1 de ellos. Una paciente abandonó el protocolo y en otra se suspendió

a las 24 semanas por persistencia de alta carga viral.

Conclusiones: La terapia con PI y RV tiene una alta tasa de respuesta de las 24 y 48 semanas y es en general bien tolerada. Esperamos los controles a las 24 semanas de su término para conocer su respuesta sostenida en estos casos.

(Protocolo EAP-BV 16209, Laboratorio ROCHE).

*Gastroenterol Hepatol 2002; 25: (S2) 28*

## Carcinoma Hepatocelular: etiología, diagnóstico y tratamiento

LC Gil, C Defilippi, D Oksenberg, J Poniachick, G Smok, I Orellana, J Gallardo, P Palavecino, J Díaz, J Brahm.  
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Antecedentes: El carcinoma hepatocelular (CHC) es la principal neoplasia maligna primaria del hígado, en un alto porcentaje se asocia a cirrosis hepática (CH) y sus etiologías. Es poco sintomático y el diagnóstico suele hacerse por imágenes y marcado-

res tumorales de seguimiento de la CH. El estado clínico de la CH y el tamaño del tumor son elementos a considerar para decidir el tratamiento (trat).

Objetivos: evaluar posibles etiologías, cuadro clínico, confirmación diagnóstica y tratamientos planteados en casos de CHC.

Material y Métodos: Revisión retrospectiva de las historias clínicas de pacientes, con diagnósticos de CHC ingresados al Hospital Clínico entre enero de 1995 a diciembre de 2000. Se evaluó sintomatología imágenes diagnósticas (ECO y TAC en todos los RNM, en 11), confirmación histológica y/o niveles de Alfafetoproteína (AFP) y los métodos terapéuticos utilizados.

Resultados: 67 pacientes edad promedio de 68 años, (rango 35-83), 49 hombres (edad promedio 65 años, rango 35-83) 18 mujeres (edad promedio 71 años. Rango 45-86), 12 (18%) ictericia y/o masa palpable, 55 (83%) se sospecharon por imágenes en el seguimiento y síntomas de deterioro de la CH. La etiología más probable fue el Alcoholismo (OH) en 25 (37%), VHC en 9 (13%), OH mas VHC en 7 (10%), VHB en 7 (10%), VHC mas VHB en 2, CBP en 1, CH por autoinmunidad 1, no precisada en 7 (10%) y en 8 (12%) casos no se documentó CH, 22 eran Child A, 16 Child B, 29 Child C. el diagnóstico se confirmó por histología en 41 (61%) AFP > a 400 en 23 (35%), en 3 se baso en imágenes de hallazgo operatorio. Por tumor mayor a 8 cms y/o CH avanzada no se hizo Trat. manteniéndose observación en 30 (45%), cirugía en 16 (24%), (resectiva en 12), Quimioembolización en 10 (12%) y Alcoholización percutánea en 6 (8%), 5 no aceptaron ningún tratamiento.

Conclusiones: En la mayoría de nuestra población el CHC se asocio a CH, EL OH, VHB fueron las etiologías más frecuentes. La principal forma de sospecha diagnóstica corres-

pondió a hallazgos imageneológicos en el seguimiento de una CH. El diagnóstico tardío de HCC y CH avanzada impidieron intentar realizar Trat. potencialmente curativos, por el cual se plantea la necesidad de un diagnóstico precoz y estudios prospectivos para evaluar nuestra realidad.

*Gastroenterol Hepatol 2002; 25: (S2) 24*

## Niveles de hemocisteína, Folato y vitamina B12 en hígado graso no alcohólico

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**Introducción:** La depleción de folato y la elevación de la homocisteína (Hcy) aumenta el riesgo de desarrollar daño hepático alcohólico u promueve el estrés oxidativo en animales. Además se ha observado una relación inversa entre niveles séricos de folato e índice de masa corporal (IMC) y una correlación positiva de Hcy y masa grasa. **Objetivo:** Determinar si existe asociación entre niveles séricos de Hcy y folato con hígado graso no alcohólico (HGNA).

**Métodos:** Se midieron los niveles séricos de Hcy, Folato vitamina B12 y pruebas hepáticas a 34 pacientes obesos sometidos a cirugía bariátrica, a las cuales se les realizó biopsia hepática durante el procedimiento quirúrgico. En el estudio histológico se cuantificó la presencia de grasa, inflamación y fibrosis en escala de 0 a 3. Se definió como EHNA un

score histológico > 0 = de 4 y esteatosis severa como grasa = 3.

**Resultados:** De los 34 pacientes, se diagnosticó EHNA en 14 casos y 16 presentaron esteatosis severa. No se observaron diferencias significativas en los niveles séricos de folato, Hcy y B12 entre aquellos con EHNA e hígado normal o con mínimas alteraciones. Sin embargo los niveles séricos de folato fueron significativamente menores (dentro de límites normales) en los pacientes con esteatosis severa (11,7 + 3,5 vs 8,9 + 3,4, p = 0.027). No se encontró diferencia en los niveles de Hcy y B12 entre pacientes con y sin esteatosis severa. **Conclusión:** 1) En esta muestra no se encontró una asociación entre niveles de Hcy, folato y B12 con EHNA. 2) Se detectó una relación inversa entre niveles de folato y esteatosis hepática. Se requieren de futuros estudios para evaluar la importancia de esta asociación. (FONDECYT N° 1010571 y N° 1011057).

*Gastroenterol Hepatol 2002; 25: (S2) 26*

## Translocación bacteriana en obesos con sobrecrecimiento bacteriano intestinal

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La obesidad es un factor de riesgo importante para la esteatosis hepática, se acompaña frecuentemente de sobrecrecimiento bacteriano intestinal (SBI) y alteración motora

intestinal, por otra parte la esteatosis hepática puede progresar desde la esteatohepatitis no-alcohólica (EHNA) a cirrosis. Múltiples son los mecanismos que contribuyen en este proceso, entre ellos la injuria mediada por la secuencia endotoxinas y citoquinas, las endotoxinas son lipopolisacáridos derivados de la pared de bacterias gram (-) de origen intestinal, que llegan al hígado a través del proceso de translocación bacteriana.

**Objetivo.** Estudiar la presencia de bacterias en los ganglios mesentéricos de pacientes obesos con SBI y correlacionar con el daño histológico hepático.

**Pacientes:** 25 mujeres y 5 hombres obesos sometidos a cirugía bariátrica, edad  $x$  34,3 (20 a 54) con IMC  $x$  de  $43,9 + 4,7$ . Se realizó en ayunas un test de H2 con lactulosa por 180 min, mediciones cada 10 min después del basal, se evaluó el tiempo de tránsito oro-cecal (TTOC) (80-100 min) y presencia de SBI (basal  $>$  de 10 ppm y/o un valor  $>$  a 10 ppm sobre el basal los primeros 60 min). Durante la cirugía se tomó muestra de ganglio mesentérico ileal para cultivo y de hígado para estudio histológico. Análisis estadístico se usó test de Fischer exacto y Anova,

**Resultados:** 12 pacientes (40%) presentaron SBI, 4 (13,3%) tuvieron cultivo de ganglio (+) para bacterias gram (-), todos en el grupo con SBI ( $p$ : 0,018). TTOC fue similar para los grupos con y sin SBI ( $112 + 6$  y  $114 + 5$  min), el grupo con ganglio (+) fue mayor no significativo ( $133 + 6,5$  m). La biopsia hepática determinó EHNA en 3 de los 4 pacientes con cultivo de ganglio (+), en 64% de los pacientes con SBI y solo en el 20% de los pacientes sin SBI ( $p$ : 0,014), **Conclusión:** Estos resultados sugieren la presencia de translocación bacteriana en pacientes obesos con EHNA, SBI y TTOC más prolongado. Estos resultados apoyarían la hipótesis de injuria hepática en

pacientes obesos con esteatosis a través de la vía SBI, endotoxinas y citoquinas.

*Gastroenterol Hepatol 2002; 25: [S2] 16*

## Relación del Gen X con HbeAg como factores pronósticos en la evolución de la infección con virus hepatitis B. Informe preliminar.

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**Introducción:** El uso de biología molecular en el diagnóstico de infección con virus hepatitis B (VHB) ha planteado nuevas interrogantes en la interpretación de estos métodos. La detección de DNA - VHB por PCR se realiza a partir de las regiones genómicas S, C y/o X, obteniéndose resultados discordantes en algunos casos. En los estudios de seguimiento de pacientes HBsAg positivo hemos detectado, en todos los casos, DNA viral al amplificar la región S. Sin embargo, no siempre se detecta DNA de la región X en la misma muestra.

**Objetivo:** Correlacionar los marcadores serológicos de VHB con la detección de DNA de las regiones S y X en la evolución de la infección.

**Metodología:** Estudio retrospectivo a partir de sueros HBsAg (+) de pacientes con diagnóstico clínico de hepatitis aguda ( $n$ : ) y crónica ( $n$ : 3) con HBeAg (+) (1ª muestra) y seroconversión posterior (2ª muestra). Se seleccionaron, además, 1 caso de hepatitis

N° Muestras	DNA S		DNA X		HBeAg
	Positivo	Negativo	Positivo	Negativo	
Positivo	12	12	0	12	0
Negativo	14	13	1*	1**	13
Total	26	25	1*	13	13

crónica con HBeAg persistente y 4 casos con anti HBe persisten (14 muestras). En todos los sueros se analizó la presencia de DNA de las regiones S y X a través de PCR (HBV Fast PHARMAGEN y PCR in house, respectivamente) y se correlacionó con la presencia de HBeAg. Resultados:

Las muestras pre y post seroconversión en los casos agudos y crónicos se correlacionaron directamente con la presencia y ausencia de DNA - X, respectivamente, así como también los casos crónicos. Las muestras discordantes corresponden a 1 caso de resolución posterior de la infección (\*) y un resultado positivo débil (\*\*).

Conclusión: Encontramos una relación directa entre HBeAg y DNA X. Dado que el gen X tendría una función transactivadora de diversos promotores virales de la replicación y expresión del genoma, podría éste tener directa relación con la síntesis de HBeAg, marcador de replicación viral activa, y con la evolución clínica de la infección. Beca Sava/ - Sociedad Médica de Investigación Clínica 2001-2002.

*Gastroenterol Hepatol 2002; 25: (S2) 20*

## Hepatitis crónica por virus C: factores asociados a la severidad del daño histológico

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Introducción: La infección por virus C es una causa de hepatitis, crónica y cirrosis frecuente en nuestro medio. Se asume que el 20% de los pacientes desarrollan cirrosis tras un seguimiento de unos 8 años, porcentaje que podría aumentar cuando se asocia a esteatosis y/o hemosiderosis en la biopsia hepática. Además la obesidad (IMC mayor de 27 Kg/m<sup>2</sup>), diabetes e ingesta alcohólica mayor de 40 g/semanal, aumentarían el daño histológico. Existen pocos estudios que hayan evaluado estos cofactores en relación a la severidad histológica.

Objetivos: Correlacionar los depósitos de grasa, fierro y los cofactores, con el grado de daño hepático según los criterios de Knodell, en pacientes con hepatitis crónica por virus C.

Materiales y métodos: Se incluyeron 84 biopsias analizadas por el mismo patólogo, que se agruparon en: hepatitis crónica con actividad leve y sin fibrosis (grupo I), hepatitis crónica con leve o moderada inflamación y fibrosis leve

(grupo II) y hepatitis crónica moderada con fibrosis severa o cirrosis (grupo III). Se analizó la presencia de esteatosis (grados 0,1,2,3) y la hemosiderosis (grados 0, 1,2,3) en la biopsia hepática. Además, se correlacionó la presencia de obesidad, diabetes mellitus y alcoholismo con la severidad histológica.

Resultados: En el grupo I hubo esteatosis en el 56% (53% grado 1 y 3% en grado 2-3), en el grupo II en el 70% (59% grado 1 y 11 % grado 2-3) y en el grupo III en el 78% (61% grado 1 y 17 % grado 2-3)(P no significativa). La hemosiderosis estuvo presente en el 18% (15%-grado 1 y 3% grado 3), 26% (grado 1 en 22%, grado 3 en 4%) y 2 (grado 1 en 4%, grado 2 en 9% y grado 3 en 9%) en los grupos I, II, III respectivamente. (P no significativa). El IMC mayor de 27 estuvo presente en el 56%, 68% y 76% para los grupo I, II y III respectivamente (P no significativa). La ingesta alcohólica > de 40 gramos/semanal se encontró en el 38%, 52% y 57%, del grupo I, II y III respectivamente (P no significativa). El porcentaje de diabéticos fue de 3%, 15% y el 30% para los grupo I, II y III respectivamente (P no significativa). Todas las diferencias no fueron significativas

Conclusiones: Esta experiencia podría sugerir que existiría una correlación: entre severidad histológica y la presencia de esteatosis en la biopsia hepática y que además, se asocia con la obesidad, diabetes mellitus e ingesta alcohólica. No observamos relación clara con la hemosiderosis. Sin embargo se necesita un mayor número de pacientes.

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## Utilidad de la Biopsia Hepática. Análisis de 1.330 casos

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La biopsia hepática (BH) es el "gold standard" para confirmar y establecer la severidad del daño de las enfermedades del hígado y no ha perdido vigencia en la actualidad, pese a los avances tecnológicos particularmente en las imágenes. Los beneficios de este procedimiento están bien establecidos en patologías autoinmunes, virales, metabólicas y congénitas entre otras. Sin embargo, su utilidad en otras enfermedades es siempre motivo de discusión.

Objetivo: Evaluar la indicación y utilidad diagnóstica de la BH en nuestro medio y la correlación entre las hipótesis diagnóstica y su resultado final.

Material y métodos: Se revisaron un total de 1.330 BH de nuestro hospital efectuadas entre los años 1984 y 2001, correspondiendo a 44,4% hombres y 56,6% mujeres, con un promedio de edad de 48 años (rango 9-82) y 49 años (rango 16-83), respectivamente. Se evaluaron los antecedentes clínicos, indicación de la BH y el informe histológico.

Resultados: Las indicaciones de la BH más frecuentes fueron: cirrosis sin etiología clara (11,5%), hepatitis crónica (8,6%), infección por virus C (8,4%), daño hepático alcohólico (8,3%), infarcto (7,4%), cirrosis biliar primaria (6,8%), estudio de tumor primario (6,1%), colestasia (6%) y otros (37,9%). Hubo confirmación diagnóstica en el 55,8%, discordancia en el 26,2%, la biopsia resultó normal en

10,3% y la muestra resultó insuficiente en el 1,3%. El 6,5% (n=86) restante, fueron por control de tratamiento o de evolución de diversas enfermedades: cirrosis biliar primaria (34), trasplante hepático (22), hepatitis crónica autoinmune (21) y hepatitis C (9).

Conclusiones: La BH continúa siendo en la actualidad una herramienta útil, y en esta experiencia, habitualmente se confirma la hipótesis diagnóstica. Sin embargo, no es infrecuente detectar enfermedades no sospechadas clínicamente.

*Gastroenterol Hepatol 2002; 25: (S2) 23*

## Desactivación de las células estrelladas del hígado y regresión de la Fibrosis hepática en pacientes con hepatitis autoinmune con terapia inmunosupresora.

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Recientemente hemos demostrado la posibilidad de una regresión de la fibrosis hepática (FH) con terapia Inmunosupresora (TI), en pacientes con hepatitis autoinmune (HAI). Por otra parte, en los últimos años se ha establecido que las células estrelladas del hígado (CEH) son las responsables de la aparición de la FH, a través de un proceso de activación, por el cual aumentan la síntesis de la matriz extracelular. La aparición de alfa actina de músculo liso ( $\alpha$ AML) en las CEH ha demostra-

do ser un marcador de su activación, siendo posible su cuantificación con técnicas inmunohistoquímicas. Existen algunos experimentos in vitro y estudios in vivo de disminución de la actividad de las CEH (desactivación), cuantificado con esta técnica.

Objetivo: investigar si la reversibilidad de la FH en pacientes (pac) con HAI tratados con TI se correlaciona con la desactivación de la CEH. Pacientes y métodos: 15 pac con HAI, edad  $40.9 \pm 14.5$  años, 80% de sexo femenino, con a lo menos 2 biopsias separadas por  $> 2$  años en su seguimiento y fueron ingresados a este estudio. Todos los pacientes fueron tratados con TI y el tamaño de las biopsias hepáticas eran  $> 10$  mm de longitud y contenían  $> 6$  espacios porta. Se comparó la longitud de la biopsia hepática basal y de control y la severidad histológica de la fibrosis, usando el parámetro respectivo del índice de Köndell (grado de fibrosis 1-4). Se cuantificó la activación de la CEH en bajo y alto grado según el número de células con  $\alpha$ AML.

Resultados: No hubo diferencias entre las longitud de la biopsia basal y de control:  $25,8 \pm 7,4$  mm v/s  $23,8 \pm 8,2$  mm. La puntuación de Knodell para la fibrosis en la biosia inicial fue  $2,75 \pm 0,93$ , la cual disminuyó a  $1,75 \pm 1,48$  en las biopsias de control ( $p < 0,05$ ). En 10 pac (67%) se comprobó una disminución de la FH y en todos ellos se demostró una disminución de la activación de las CEH, desde alto a bajo grado o nula activación; en 2 pac existió una progresión de la FH, la cual se acompañó de un aumento de la activación de las CEH; en 3 pac no existió cambios en la FH ni en la activación de las CEH.

Conclusión: La TI puede lograr una regresión de la FH en HAI, la cual es proporcional a la desactivación de las CEH.



## Hígado graso no-alcohólico: características clínicas e histológicas

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El hígado graso no alcohólico (HGNA) es una entidad clínico-patológica de reciente reconocimiento. Sus características clínicas y de laboratorio no han sido completamente establecidas y su etiopatogenia aún es desconocida.

Objetivos: Describir los hallazgos clínicos, de laboratorio e histológicos en pacientes con HGNA.

Pacientes y métodos: Se revisaron 120 pacientes (pac) con esteatosis macrovesicular e inflamación lobulillar con o sin fibrosis demostrada por biopsia. Se excluyeron pacientes con ingesta alcohólica > a 40 gr/semanal, portadores de hepatitis B o C. Se analizaron en forma retrospectiva las características clínicas (edad, sexo, factores asociados, síntomas), hallazgos ecográficos, exámenes de laboratorio y la biopsia hepática.

Resultados: La edad x de los pac fue 48,9 + 15,6 años. 66% de los cuales eran mujeres. Los factores asociados fueron: 71% sobrepeso u obesidad, 48% hipertrigliceridemia, 37% hipercolesterolemia, 27% diabetes, 6% enfermedad celíaca y 10% no tenían factor asociado. Las manifestaciones clínicas que motivaron la consulta fueron: 22% dolor abdominal en HD, 23% decaimiento o fatiga, 8% prurito y 48% fueron asintomáticos. En el labora-

torio 26% tenían bilirrubina elevada (1,1 + 1,18 mg/dl, valor máximo de 8,4 mg/dl), 69% tenían elevación de SGPT (2,5 + 3,5 veces sobre el valor normal (VN), valor máximo 22 veces), 48% tenían elevación de SGPT (1,5 + 1,2 veces sobre el VN, valor máximo 6,7 veces), 68% tenían elevación de FA (1,7 + 1,6 veces; sobre: 1:1 valor normal, valor máximo de 12,3 veces) y 52% tenían elevación de GGT (1,7 + 1,6 veces sobre el VN, valor máximo de 10,9 veces). La ecotomografía abdominal fue compatible con infiltración grasa hepática en el 65% de los pac. La biopsia hepática mostró esteatohepatitis en el 50%, esteatohepatitis con fibrosis en el 40%, de los casos y 10% tenían además cirrosis.

Conclusiones: Esta serie confirma que la mayoría de los pac con HGNA son del sexo femenino y el factor de riesgo asociado más importante es la obesidad. Una proporción importante tiene fibrosis y/o cirrosis. Existe un subgrupo de pac con HGNA sin factor de riesgo asociado, que podrían ser catalogados como HGNA criptogénica.

## Papel del Citocromo P450 2E1 en la progresión del hígado graso no-alcohólico asociada a obesidad.

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El Hígado graso no alcohólico (HGNA) es una entidad de alta prevalencia. sus características histológicas son muy semejantes a la enfermedad hepática alcohólica, sin que exista el antecedente de la ingesta de alcohol. Sus mecanismos etiopatogénicos son aún desconocidos. Se ha postulado que la inducción del citocromo P450 (CYP) 2E 1, frecuente en la enfermedad hepática alcohólica, podría tener un papel en la patogenia de esta entidad. favoreciendo el estrés; oxidativo y la lipoperoxidación.

Objetivo: Determinar la relación entre la inducción del CYP 2E1 y la progresión del HGNA en pacientes obesos.

Pacientes y métodos: Se estudiaron 48 pacientes obesos sometidos a cirugía bariátrica y 6 pacientes con normo peso sometidos a cirugía abdominal. Durante la cirugía se realizó una biopsia hepática a partir de la cual se gradúo la severidad histológica y se preparó la fracción microsomal por ultra centrifugación diferencial. Se determinaron los contenidos de CYP total y del CYP 2E1 a través de fotometría y Western Blot (WB) respectivamente, en el microsoma hepático. Se

compararon los valores densitométricos del WB entre los pacientes con normo peso e histología hepática normal (N) con pacientes con esteatosis pura (E), con esteatosis mas inflamación (EI) y fibrosis (F) y se calculó la relación CYP 2E1/CYP total.

Resultados: Las densitometrías del CYP 2E1 fueron: 1,01 + 0,20 en pacientes N (n = 6), 1,45 + 0,14 en E (n = 21 ), 2,25 + 0,28 en EI (n = 13) y 2,27 + 0,32 en F (n = 14). Los pacientes que presentaron EI y/o F en comparación con los pacientes con E o N tuvieron valores del CYP 2 E1 significativamente mayor (p < 0.05).

Conclusiones: Un aumento del contenido del CYP 2E1 en pacientes con EI y F podría tener un papel en la progresión del HGNA asociada a obesidad. Se sugiere que este hecho podría condicionar un aumento del estrés oxidativo.

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## Composición de los ácidos grasos de los lípidos del hígado y del tejido adiposo de mujeres obesas con hígado graso no-alcohólico

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La patogenia del hígado graso no alcohólico (HGNA) es aún desconocida y frecuentemente se le asocia con obesidad.

Objetivos: Analizar el perfil de los ácidos grasos de los lípidos hepáticos, del tejido adiposo subcutáneo (abdominal) y el nivel de las lipoproteínas plasmáticas de mujeres obesas con HGNA.

Pacientes y métodos: Se estudiaron 17 pacientes obesas con un IMC mayor de 35 kg/m<sup>2</sup>, sometidas a cirugía bariática y 6 mujeres controles de edades comparables y con un IMC normal sometidas a cirugía abdominal. La composición de los ácidos grasos de los lípidos se analizó por cromatografía gaseosa y se midió el perfil lipídico del plasma.

Resultados: Respecto de los controles, el HGNA se asoció con un aumento significativo porcentual en hígado de los ácidos palmitoleico ( $3,65 \pm 2,3$  vs  $0,33 \pm 0,10$ ), oleico ( $18,9 \pm 7,4$  vs  $11,2 \pm 1,8$ ) y linoleico ( $11,3 \pm 5,9$  vs  $0,60 \pm 0,10$ ) y una disminución de los ácidos grasos poliinsaturados de cadena larga (AGPICL)

araquidónico ( $0,99 \pm 0,80$  vs  $7,32 \pm 1,40$ ), eicosapentaenoico ( $0,30 \pm 1,04$  vs  $2,23 \pm 0,80$ ) y docosahexaenoico ( $0,83 \pm 0,60$  vs  $9,23 \pm 1,20$ ). El tejido adiposo subcutáneo abdominal de las obesas con HGNA exhibió un aumento de los ácidos grasos saturados ( $62,9 \pm 12,9$  vs  $42,1 \pm 3,0$ ) y del ácido linoleico ( $11,28 \pm 5,90$  vs  $0,60 \pm 0,10$ ) y una marcada disminución del ácido 00-linoleico ( $0,69 \pm 0,09$  vs  $1,90 \pm 0,40$ ). No se observaron cambios en el perfil de las lipoproteínas plasmáticas entre los grupos. Conclusión: La disminución de los AGPICL n-6 y n-3 en el hígado y el aumento de la relación n-6/n-3 en el tejido adiposo subcutáneo abdominal en las mujeres obesas con HGNA permitiría sugerir que una mejor oxidación y/o una mayor síntesis de ácidos grasos contribuiría a explicar el mecanismo de la esteatosis del HGNA.

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## Cirrosis biliar primaria: experiencia en doce años

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Introducción: La cirrosis biliar primaria (CBP) es una enfermedad colestásica crónica progresiva, que hemos observado con mayor frecuencia en los últimos años, como importante causa de hepatopatía crónica e hipertensión portal.

**Objetivo:** Analizar las características clínicas, de laboratorio e histológicas de pacientes CBP.

**Métodos:** Se revisaron retrospectivamente las fichas clínicas de pacientes con diagnóstico histológico de CBP confirmado por el mismo patólogo, en el período de enero de 1990 a diciembre del 2001.

**Resultados:** Se evaluaron 110 casos, 106 de sexo femenino (96%) con una edad media de 52 años (rango 30 a 76). Al momento de presentación, había prurito en el 69% de los casos, astenia en el 62%, hiperpigmentación en el 31%, hepatomegalia en el 24%, ictericia en el 18% y xantomas-xantelasmas en 6%. Se encontraron signos de hipertensión portal con ascitis en un 9%, esplenomegalia en un 11% y várices esofágicas en un 28%. Los exámenes de laboratorio mostraban aumento de fosfatasas alcalinas entre 1.5 a 12x de GGT 1.5 a 40x, aminotransferasas hasta 12x, bilirrubina total hasta 12x y una albúmina promedio de 3.5 (rango 1,8 a 4,6). Había títulos aumentados de anticuerpos anti-mitochondriales en el 56% de los casos, antinucleares en 35%, anti-músculo liso 28% y elevación de IgM en un 71%. Se asociaron otras enfermedades autoinmunes como Sjören en 38%, hipotiroidismo en 13%, esclerodermia en 7%, artritis reumatoidea en 5%, Raynaud en 4%, enfermedad celíaca y sarcoidosis en un caso y otras patologías aisladas. La biopsia hepática demostró CBP en etapa I en un 12% de los casos, etapa 2 en un 29%, etapa 3 en 45% y etapa 4 en 14%. El tratamiento fue mayoritariamente con ácido ursodesoxicólico (URSO) y se realizó trasplante hepático en 8 pacientes, por hemorragia digestiva recurrente y prurito intratable como principal indicación.

**Conclusión:** La CBP se diagnostica con mayor frecuencia en nuestros centros, constitu-

yendo una causa importante de hepatopatía crónica y en asociación frecuente con otras enfermedades autoinmunes. Su tratamiento con URSO y evolutividad deben estudiarse en trabajos prospectivos desde estadios más precoces en el diagnóstico, siendo el trasplante la alternativa terapéutica en casos avanzados.

*Gastroenterol Hepatol 2002; 25: (S2) 9*

## Encefalopatía hepática crónica: relación con los niveles de manganeso y lesiones en los ganglios basales en la resonancia nuclear magnética cerebral.

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La encefalopatía hepática crónica (EHC) es una compleja manifestación del daño hepático crónico (DHC). Hay algunas evidencias clínicas recientes que sugieren el rol de manganeso (Mn) en la patogénesis de la alteración y que podría explicar la hiperintensidad de los ganglios basales que se ve en la resonancia nuclear magnética cerebral (RNM). Pocos estudios han documentado niveles elevados de Mn en sangre y líquido cefalorraquídeo (LCR) en estos pacientes.

**Objetivo:** Estudiar las características clínicas de la EHC y severidad del daño hepático en pacientes con DHC, y su asociación con los

niveles de Mn y alteraciones en la RNM cerebral.

Métodos: Se estudiaron pacientes con EHC evaluados inicialmente en neurología sin daño hepático conocido y cirróticos en control con algún desorden del movimiento. A todos se les midió el nivel de Mn sérico y realizó una RNM cerebral. A dos de ellos se les investigó además el Mn en el LCR.

Resultados: Se incluyeron doce pacientes con DHC que presentaban parkinsonismo, corea o desórdenes psiquiátricos, con las siguientes etiologías: etilismo crónico en 6 casos, hepatitis C en 1, enfermedad de Wilson en 1, cirrosis biliar primaria en 1 y 3 criptogénicas. Cuatro pacientes tenían score de Child-Pugh C, siete B, y sólo uno A. Todos presentaron niveles de Mn elevados en sangre, promedio 12,6 ug/dl (rango 0,3-26, VN < 0,06). En los dos en que se midió en LCR, el Mn fue de 2,9 y 3,3 ug/dl (VN < 0,45 ug/dl). Se observó un patrón característico a la RNM en T1, con hiperintensidad simétrica de ganglios basales en todos los pacientes, lo que incluso orientó al estudio de DHC en 6 de ellos.

Conclusiones: Nuestro estudio apoya la hipótesis de que el Mn tendría un rol patogénico en la EHC y que la RNM puede confirmar la repercusión metabólica cerebral. Sin embargo, se requieren estudios mayores y con grupo control, que permitan evaluar esta alteración y el eventual uso de una terapia quelante.

## Genética

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*XXXVIII International Congress on the history of Medicine 2002; Abstract Book: p111.*

### History of the Chilean welfare state in XX Century

Cruz Coke R

At the beginning of the XX century Chile was an undeveloped nation with 3 million people (70% rural), without public health organization and very low standard of living; with life expectancy of 40 years of age and infant mortality 30%. The dedicated work of a select group of medical reformers pioneered, between 1918 to 1952 a public policy of radical social medical and health changes. Sanitary code act (1918), Social Security and Labor acts (1924), Institute of Bacteriology (1929), National Council of Nutrition (1937), Preventive Medicine Act (1938), Maternal and Child Care Act (1938), School of Public Health (1945) and National Health Service (1952). In 1960 Chile has reached an advanced level of a welfare state, with a socialized medicine covering 95% of hospital beds, 90% of medical doctors and 85% of live births. In 1970 primary health care covers 98% of children and Chilean population have an 87% of permanent dwellings, 80% of electricity and life expectancy of 62 years. During the last quarter of the century, Chile has experienced a series of social changes under different political and military governments that led to the complement of the welfare state with neoliberal and private medical policies. Consequently at the end of the XXth century, Chile with 15 million population (85% urban) was able to reach the characteristics

of a middle developed nation with the best health indicators of vital statistics such as life expectancy of 75 years of age, 1% of infant mortality, 99% of deliveries in health facilities and full primary preventive health care. Moreover the country has eradicated the WHO classical infection diseases such as leprosy, malaria yellow fever, new born tetanus, measles and cholera. Chile has been a good example of success of the welfare state to solve social and health shortages in undeveloped nations.

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## Cytogenetic diagnosis of gonadal dysgenesis in child and adolescent women

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### Introduction

Gonadal dysgenesis is the end stage of a process of follicular atresia <sup>(1,2)</sup>. The Turner syndrome is the most common cause with an incidence of 1 in 2500 female births <sup>(3)</sup>. We report the experience obtained in 105 child and adolescent women, younger than nineteen years in the Clinical Genetic Unit, Hospital Clínico Universidad de Chile, in a period of twenty years. We present the principal chromosomal anomalies found in the

cytogenetic study in these patients so as the principal clinical characteristics.

### Objective

The objective is to describe and to analyze the principal cytogenetic findings in young and adolescent girls patients with gonadal dysgenesis, emphasizing the importance of this evaluation in the diagnosis and investigation of this pathology.

### Patients and methods

We compiled the clinical indexes and the outcome of the karyotype in 105 patients younger than nineteen years between March of 1981 and December of 2001. All the patients were referred for cytogenetic diagnosis to the clinical Genetic Unit of the hospital Clínico Universidad de Chile in Santiago de Chile.

The chromosomal study was done in lymphocytes of venous blood sample, cultivated in enriched medium with addition of mytogen for 72 hours at 37° Celsius. The analysis was realized by means of Giemsa banding (GTG), what allows to individualize the chromosomes and recognize structural alterations. As a minimal, 30 mitosis were counted. If one aneuploid cell was found, the cell chromosome count was increased up to 100 cells <sup>(4,5,6)</sup>

### Results

In the study period, we found 105 patients. 46% presented aneuploidy of one chromosome X with 45,X karyotype. A 54% presented X chromosome mosaics, in this group we didn't find patients with cellular lines with Y chromosome,

In relation to the origin of the derivation, 77% proceed of the Metropolitan Region and the 23% of the rest of the Country.

The age at cytogenetic diagnosis was less than 14 years in 79% of the patients, in 27% the diagnosis was established before the 5 years,

Only 16 patients were diagnosed during the first year of life,

The principal reason of derivation were; 60% of the cases because of Turner phenotype. 15% for short stature 7,6 % for gonadal dysgenesis 4.8% for psychomotor developmental delay, 2.9% for ovaric insufficiency, Two patients were derived for delayed puberty, one for suspicion of genophaty, one for amenorrhea, one for submucose fissure palate and one patient for cardiac anomalies, In 4 we ignore the motive of derivation, In relation to the psychomotor development. it was evaluated in 73 patients. the 70% of them presented normal development and 30% had delayed psychomotor development, In 71 patients the gestational age at childbirth was consigned, with antecedent of premature delivery in 17%.

In most cases there were not family antecedents of consanguinity or gonadal dysgenesis. In the patients in which the characteristic phenotype was consigned. the results were; 48 patients presented high arched palate, 39 patients had prominent and anomalous rotated auricles. 38 had broad chest. 37 had separated and hypoplastic nipples. 38 had cubitus valgus. 31 had hypoplastic and hyper-Convex nails and 15 presented short fourth metacarpals,

In 8 patients alterations cardiac were consigned for means of echocardiography. Three patients carried coarctation of the aorta, three had bicuspid aortic valve, one had aortic valvular stenosis and one patient presented interauricular communication.

#### Discussion

Effective management of patients with ovarian dysgenesis depends on a proper and early diagnosis for means of cytogenetic evaluation with anticipation of the anatomical and endocrinological consequences in relation

to the productive potential in these patients<sup>(1,7,8)</sup>. Counseling and adequate support on psychosocial field must be given to all of them.

In these patients it is very important to discard or confirm on cellular line containing a Y chromosome.

Patient carriers of a Y chromosome, are at risk for development of gonadal neoplasm and should receive adequate and suitable treatment<sup>(8,9)</sup>. Besides, in this patients, it is recommended to analyze the presence of SRY gene (sex determining region on the Y), through techniques of molecular evaluation the test of the polymerase chain reaction (PCR)<sup>(9)</sup>.7. Saenger P, Albertsson K, Conway G, Davenport M, Gravholt C, Hintz R, Hovatta O, Hultcrantz M, Landin-wilhelmsen K, Lin A, Lippe B, Paquino A, Ranke M, Rosenfeld R, Silberbach M.

## Medicina Nuclear

World Journal of Nuclear Medicine 2002; 1: S323 (S2).

# Gammacamera compared to conventional Probe thyroid uptake using I-131

Alay R, Padilla P, Alliende I, Otarola S, Garcés N, Lillo R, González P, Estefanía F, Vidal J.

Center of Nuclear Medicine of Clinical Hospital of University of Chile.

The aim of the study was to correlate the results of the percentage of thyroid uptake (TU) with external detector type probe (PED) and a gammacamera (GC).

Our hypothesis was that there are no significant differences between both measurements.

In 91 patients (mean age  $\pm$  SD =  $41 \pm 13$ ; 77 women and 14 men) 24 hours % TU in both equipments was obtained, with the standard technique of our laboratory.

Results were as follows:

Table 1. Quantitative results of % thyroid Uptake using a Probe (PED) and gamma camera(GC)

Conclusions:

Correlation was excellent. However there are significant difference between mean of both groups, GC values are higher than probe measurements. The difference is greater in those with less than 10% TU. Very interesting, there was no difference in the group with  $>10\%$ TU.

In clinical practice it is possible to perform the %TU measurement using a GC, taking into account the limitations noted above.

% TU	n	%mean $\pm$ SDPED	%mean $\pm$ SDGC	p*
% TU > 10	69	36.99 $\pm$ 23.10	38.14 $\pm$ 23.63	0.0605
%TU $\leq$ 10	22	3.55 $\pm$ 3.31	4.95 $\pm$ 3.64	0.0006
%TU total	91	28.90 $\pm$ 24.74	30.12 $\pm$ 25.06	0.01

\* n-2 degrees of freedom(Student paired t test)



# Bone scan in the diagnosis and management of acute osteoarticular infection in children

C Coll, T Massardo, JL Cifras, H Moya, MA Verdugo, F Soza.

## Introduction

One of the most important causes of children residual damage in the skeleton in Chile are untreated or treated incompletely osteoarticular infections (OAI). The goal of this study was to assess the value of emergency in-hospital pediatric three-phase bone scan in the evaluation of OAI.

## Methods

The inclusion criteria were: a) high clinical suspicion of acute OAI and b) a suspect of a secondary localization in a known recent OAI. In this prospective study the gold standard was the final diagnosis at discharge. Thirty-eight children were studied with 54 triphasic bone scans using MDP-Tc99m; some with 4<sup>th</sup> phase. The population mean age was  $4 \pm 5$  years, 66% of them male. Nine children had their first scan prior to surgical intervention (5 of them had also a posterior follow-up scan) and 17 had a post surgery scan (within a median of 5 days ranging from 1 -34 days after surgery). Twelve cases were not submitted to surgery.

## Results

The global analysis showed 28 cases principally articular and 9 osteomyelitis. The most common germ observed were staphylococcus aureus (37%) and staphylococcus coagulase negative (37%), less common was streptococcus (11%); the hip was affected in 41 % of the cases, and less frequently knee

and femur. Nine patients with preoperative scans were positive with 16 locations foci. Eighty four % of them were confirmed by surgery/culture (true positive) and surgery was performed within 24 h. There were 3 lesions detected in 2 of the patients with no clinical confirmation (16% false positive). There were not any true negative with surgical confirmation in this group, even though, in 2 clinically suspected sites the bone scan were negative and the patients follow-up was not suggestive of infection in those additional localization. Seven children have negative bone scans (without surgery requirement) that did not present posterior clinical symptomatology in the follow-up up to 3 m. In 5 other cases the vascular phase demonstrated only soft tissue involvement (cellulites and phlebitis), with normal osteoblastic phase; they were treated non-invasively. In 14/17 (82%) cases evaluated post surgical intervention, it was observed agreement between the scan and the clinical evolution. In two of those cases the bone scan was negative at the initial site but a new localization was found.

## Conclusion

The three-phase bone scan is a helpful tool in the diagnosis and evaluation of acute OAI in pediatric population, mainly in the initial stages. A positive three-phase bone scan is highly accurate for OAI and a negative one rules it out securely.

# A comparison of extension and severity of perfusion, glucose metabolism and wall motion abnormalities in recent myocardial infarction on patients with and without revascularization.

Gonzalez P<sup>(1,2)</sup>, Massardo T<sup>(1)</sup>, Yovanovich J<sup>(3)</sup>, Coll C<sup>(1)</sup>, Redondo F<sup>(1)</sup>, Jofre J<sup>(1)</sup>, Chamorro H<sup>(4)</sup>, Humeres P<sup>(2)</sup>, Sierralta P<sup>(1)</sup>.

<sup>(1)</sup> Department of Nuclear Medicine of the University of Chile Clinical Hospital, <sup>(2)</sup> Department of Nuclear Medicine of Santa Maria Clinic, <sup>(3)</sup> Cardiovascular Center of the University of Chile Clinical Hospital, <sup>(4)</sup> Cardiovascular Center of Santa Maria Clinic.

**Aim:** To compare the extension and severity in perfusion, glucose metabolism and contractility abnormalities in recent myocardial infarction, assessed by different imaging modalities, and to evaluate these functional parameters in patients with and without revascularization (REV).

**Materials and methods:** We assessed 49 patients with a first MI ( $58 \pm 12$  years; 82 % males) using 1) [Tl201] rest SPECT, 2) [Tl201] redistribution (red) SPECT, 3) [F18]FDG SPECT and 4) 2D echocardiograms at a mean of 9.2 days, range: 1-24; 29 (59%) patients had been REV by means of PTCA or CABG and 20 (41%) underwent only medical therapy. All had angiogram. Images were analyzed blindly, employing the same polar map which included 17 segments in the four sets of studies. Both, the number of segments involved and their severity (normal, mild, moderate or markedly abnormal) using a

semiquantitative score from 1 to 4 were tabulated.

**Results:** In the total group (n=833 segments), the abnormal segments in echo were 302 (36%), in Tl rest 231 (28%), in Tl red 223 (26%) and in FDG 202 (24%), ( $p < 0.001$  echo vs all other). Regarding severity score, the median (s.d.) values were: 2.6 (0.5); 2.9 (0.9); 2.8 (1.2) and 2.9 (1.2), respectively ( $p < 0.01$  echo vs all other). In REV patients (n=493), the lesion size was 154 segments (31%), 116 (23%), 112 (23%) and 100 (20%), respectively. In those without REV (n=340) the number of abnormal segments were 148 (44%), 115 (34%), 111 (33%) and 102 (30%) respectively ( $p < 0.004$ , REV vs no REV). McNemar, Student t tests were used in the comparisons. The following table shows the severity score results in the 2 groups.

	REV	No REV	p
Echo	2.4 (0.5)	2.8 (0.4)	0.006
Tl rest	2.8 (1.0)	3.3 (0.6)	<0.0001
Tl red	2.5 (1.4)	3.2 (0.7)	<0.0001
FDG	2.7 (1.3)	3.4 (0.6)	<0.0001

**Conclusion:** In recent MI, echo abnormalities were bigger in size (up to 13%) than the perfusion and metabolic defects, but less severe (down to 10%) compared to radionuclide procedures, possibly due to stunning. Non REV patients presented with greater extension (up to 11%) and more severity (up to 22%) than REV ones in any of the imaging modalities, explained by therapy effect. Both, echo and radionuclide techniques appear adequate to demonstrate revascularization benefit.

# Extension and Severity of Perfusion, Glucose Metabolism and wall motion in recent myocardial infarction in patients with and without revascularization.

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University of Chile and Clinica Santa Maria, Santiago, Chile.

**Objectives:** The goal of this research was to compare the extension and severity in perfusion, glucose metabolism and contractility, assessed by different imaging modalities in patients with recent myocardial infarction (MI) with and without revascularization (REV).

**Methods:** We assessed 49 patients with a first MI (58 ± 13 years; 82% males) using 1) [Tl201] rest SPECT, 2) [Tl201] redistribution (red) SPECT, 3) [F18]FDG SPECT and 4) 2D echocardiograms at a mean of 9.2 days, range: 1-24; 29 (59%) patients had been REV by means of PTCA or CABG and 20 (41%) underwent only medical therapy. All had angiogram. Images were analyzed blindly, employing the same

polar map which included the 17 segments in the four sets of studies. Both, the number of segments involved and their severity (normal, mild, moderate or markedly abnormal) using a semiquantitative score from 1 to 4 were tabulated.

**Results:** In the total group (n=833), the abnormal segments in echo were 302 (36%), in Tl rest 231 (28%), in Tl red 223 (26%) and in FDG 202 (24%). In patients with REV (n=493), they were abnormal in 154 (31%), 116 (23%), 112 (23%) and 100 (20%), respectively. In those without REV (n=340) the number of abnormal segments were 148 (44%), 115 (34%), 111 (33%) and 102 (30%) respectively (p<0.002, REV vs no REV). The following table shows the results in the 3 groups.

**Conclusion:** The extension and severity of motion abnormalities were greater than the perfusion defect size in [Tl201] rest, [Tl201] red and FDG, in the whole group and in non revascularized patients (p<0.001). In the revascularized group there was significant difference in extension (all groups) and severity (only in [Tl201] rest vs echo). In addition, there was also a significant difference between [Tl201] rest and FDG in the total group in regard to abnormality extension (p<0.05). There was significant less severity (p<0.005) (and extension 10% ¿?) in revascularized segments as compared to non revascularized in all, but especially evident with nuclear medicine procedures.

	Extension (mean ± s.d.)			Severity (mean ± s.d.)		
	REV	No REV	Total	REV	No REV	Total
Echo	5.3 ± 3.8	7.4 ± 3.7	6.1 ± 3.8	2.4 ± 0.4	2.7 ± 0.3	2.5 ± 0.4
Tl rest	4.0 ± 2.7	5.8 ± 2.7	4.7 ± 2.8	2.8 ± 1.0*	3.2 ± 0.5*	2.9 ± 0.8
Tl red	3.9 ± 2.8	5.6 ± 2.8	4.5 ± 2.9	2.5 ± 1.3*	3.2 ± 0.5*	2.8 ± 1.1
FDG	3.4 ± 2.5	5.1 ± 2.5	4.2 ± 2.7	2.6 ± 1.3*	3.3 ± 0.5*	2.8 ± 1.2

\* p<0.0001

# Body composition and bone mineral mass in normal and obese female population using dual X-Ray absorptiometry.

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It has been observed that a greater percentage of body fat is associated with augmented bone mineral mass. Objective: The goal of this work was to assess the relationship between bone mineral density (BMD in g/cm<sup>2</sup>) and content (BMC in g) and soft tissue components, fat and lean mass (in g) in whole body of adult female population in Chile. Method: We studied 185 volunteers, asymptomatic, excluding those using estrogens, regular medication, tobacco (>10

cigarettes/day), excessive alcohol intake or with prior oophorectomy. They were separated in 111 pre and 74 post menopausal and according to body mass index (BMI) they were 37 women > 30 kg/m<sup>2</sup> and 148 <30 kg/m<sup>2</sup>. A Lunar Dual X-Ray absorptiometer was used to determine whole BMD and BMC. Results: Post menopausal women were older and smaller [p:0.0001], with higher body mass index [p:0.0007] and with lower BMD and BMC and higher fat mass than the pre menopausal group; see TABLE. In the whole group, women with BMI ≥30 (obese) were compared with normal weight observing no difference in BMD. The fat mass incremented significantly with age. Obese women > 50 years presented greater BMC than the non-obese. The percentage of fat corresponded to 48% in the obese group and to 39% in the non-obese [p<0.0001].

Conclusion: Fat mass somehow protect bone mineral loss in older normal population, probably associated to multifactorial causes including extraovarian estrogen production. Postmenopausal women presented lower mineral content than premenopausal, as it was expected.

STATUS	Age (years)	BMD (g/cm <sup>2</sup> )	BMC (g)	Fat mass (g)	Lean mass (g)
premenopause	40±9	1.147±0.069	2294±261	23999±6709	35615±3909
postmenopause	59±12	1.056±0.087	1983±258	26632±7501	34633±3799
p	0.04	<0.0001	<0.0001	0.014	ns

BMI	Age	BMD (g/cm <sup>2</sup> )	BMC (g)	Fat mass (g)	Lean mass (g)
<30kg/m <sup>2</sup>	47±12.	1.105 ±0.087	2165±306	22479±5093	34640±3332
>30kg/m <sup>2</sup>	51±13	1.132 ±0.081	2182±136	35125±5003	37371±5179
p	ns	ns	ns	<0.0001	0.0001

## Value of myocardial perfusion SPECT in pediatric population.

Massardo T<sup>(1)</sup>, Coll C<sup>(1)</sup>, Prat H<sup>(1)</sup>, Doggenweiller P<sup>(2)</sup>, Castillo ME<sup>(3)</sup>, Solis A<sup>(4)</sup>, Gonzalez P<sup>(1)</sup>.

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Isotopic myocardial perfusion studies are less frequently used in children than in adults and their indications are also different. Our goal was to analyze retrospectively the experience with stress perfusion myocardial SPECT in pediatric population. Method: Since 1998 to 2001, ten studies were performed to 5 girls and 3 boys. Their mean age was  $7 \pm 3$  years ranging from 1-11. Three of them presented abnormal coronary arteries pre and post surgical intervention with or without coil; three had Kawasaki disease with coronary aneurysms and the other two, congenital cardiopathies (Cantrell pentalogy and great vessel transposition, both with posterior left ventricular hypokinesia post surgery). Stress was obtained using dipyridamole infusion (0.56 mg/kg) in 6 cases and treadmill exercise using Bruce protocol in 4. All those tests were well tolerated. Sestamibi Tc99m was selected in 80% of the cases and Tl 201 in the rest. Only 2 small children required anesthesia during SPECT acquisition. Results: Stress EKG did not demonstrated ischemia in any case. Coronary angiography was performed only in 50% of the patients, it was concordant with SPECT features in all, two of those patients presented transient perfusion defects (one Kawasaki and one abnormal coronary artery with a fistulae). The repaired pentalogy presented ischemia and septal infarction; in that patient echocardiographic hipokinesia

was concordant with fixed hypoperfusion. One case with abnormal coronary plus mitral regurgitation (without isotopic ischemia) was submitted to embolization posteriorly, obtaining motion improvement. Clinical outcome was concordant with the presence or absence of isotopic ischemia in the rest of the patients. Conclusion: SPECT myocardial perfusion was helpful in the therapeutic approach and in prediction of outcome in children.

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## Biological distribution of reactor produced <sup>18</sup>F-FDG. Local experience.

MP Sierralta, T Massardo, MC Gil, M Chandia N Godoy, F Troncoso, MJ Jofre

### Introduction

Quality control through an animal model that relates bio distribution of a substance is fundamental prior to using it in human beings. For the evaluation of myocardial viability after recent myocardial infarction, the use of reactor produced <sup>18</sup>F-FDG (a radiotracer usually obtained in cyclotron) is proposed, production of which had never been attempted in our country.

The aim of the study was to compare the specific activities found in the different tissues after the injection of this reactor produced radiopharmaceutical with those obtained by others authors with cyclotron <sup>18</sup>F-FDG.

### Material

WISTAR female white mice, mean weight  $25,28 \pm 1,09$  g (23,8-26,9 range) in standard support conditions was used. 1,22 MBq (33 mCi) of <sup>18</sup>F-FDG were injected in a lateral tail vein.

Previously anaesthetized with Chloroform, the animals were sacrificed by jugular section at 5, 30 and 60 minutes intervals post injection.

Blood and organs were removed (liver, lungs, heart, brain, urine plus bladder, kidneys, femur, muscle and quivers), placed in vials, then weighted, and finally taken to a Gamma Packard Minaxi y Auto-gamma 5000 serie counter to obtain the counts per minute (cpm) (previously the empty vials were weighted too).

At same time, STANDARDS (STD) ( 3 dilutions) cpm and BACKGROUND (BKG) cpm were collected. We calculate 1) mean BKG cpm, 2) mean STD cpm, who then were corrected by decay factor and dilution , and 3) each one of the tissues cpm, that then were corrected by decay factor, divided by the corresponding dilution cpm and multiplied by 100 to obtain the Injected Activity % (IA%).

Finally, the IA% was divided by the tissue weight and get the Specific Activity (SA). Mean and standard deviation for each tissue at the 3 intervals were calculated.

#### Results

The uptake distribution at 30 and 60 minutes were similar between reactor and cyclotron produced  $^{18}\text{F}$ -FDG, with significant bigger SA in heart and brain respect of the rest organs. There were significant differences of SA in many organs, between the authors and between them and our results, except at the heart.

#### Conclusion

No statistically significant differences in the critical organ in study (heart) were found. Hence, local reactor produced  $^{18}\text{F}$ -FDG is a useful radiotracer in cardiac cellular metabolism assessment.

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## Isolation time determination of patients with differentiated thyroid carcinoma treated with therapeutic doses of $^{131}\text{I}$ radioiodine.

MP Sierralta, R Lillo, T Massardo, MJ Jofre.

#### Introduction

The coadyuvant treatment with  $^{131}\text{I}$  had proven to be useful in patients with differentiated thyroid carcinoma (DTC). Due to the physical characteristics of this radioisotope these patients must be absolutely isolated in order to reduce the radioactive exposure to other individuals.

The aim of the study was to determine the time required to reach the maximum permissible radiation exposure level (0,25mR/h) to general public.

#### Material

Between August 1999 and May 2000, 30 patients with DTC diagnosis in the University of Chile Clinical Hospital Nuclear Medicine Centre were studied, 25 women (83%) and 5 men (17%), mean age 45 years old (15-71 range). Tumoral histology was 86% papillary and 14% follicular types. Thirty one doses of  $^{131}\text{I}$  were administered ( one patient received 2 doses): 24 of 100 mCi (77%), 5 of 150 mCi (16%) and 2 of 200 mCi (7%); afterwards the 1 m exposition rate in air was measured at neck level with a Geiger-Müller detector. The procedure was repeated on day 4 and every day following until the predicted radiation exposure levels were reached.

## Diagnostic value of early 99m-Tc metilendiphosphonate scintimammography in the assessment of palpable breast tumors.

Results: The average exposure rate at day 0 (after given the radiopharmaceutical) was 20,12 mR/h (4-32 range). At day 4 the average rate was 0,21 mR/h (0,08-0,34 ), and 61% (n=19) of the patients reached 0,25 mR/h within that day. On day 5 10% (n=3) reached 0,25 mR/h (0,25-0,26), on day 6 16% (n=5) reached 0,25 mR/h (0,2-0,28), on day 7 6% (n=2) reached 0,39 mR/h (0,25-0,48) and the remaining 7% on day 13 and day 17 (n=2).

Patients (n)	<sup>131</sup> I/24 h uptake	Expositon rate on day 4
6	< = 2%	0,21 +/- 0,06 mR/h
4	> 2%	0,725 +/- 0,44 mR/h

Conclusion: After a treatment dose of 131 iodine over 60% of the cases can finish the isolation on day 4, and 90% on day 7. The measurement of <sup>131</sup>I uptake after 24 hours will help to determine the evolution of post treatment levels.

Massardo T<sup>(1)</sup>, Alonso O<sup>(2)</sup>, Zhu H, Ravishankar U, Maunda K, Kabasakal L, Morales R<sup>(3)</sup>, Gonzalez P<sup>(1)</sup>, Padhy AK<sup>(4)</sup>. <sup>(1)</sup>University of Chile Clinical Hospital, Nuclear Medicine Center, Santiago, Chile, <sup>(2)</sup>University of Uruguay Clinical Hospital, Nuclear Medicine Center and Oncology Department, Montevideo, Uruguay, <sup>(3)</sup>Peruvian Institute of Nuclear Energy, Neoplastic Diseases Institute, Lima, Peru, <sup>(4)</sup>Nuclear Medicine Section, Department of Human Health, International Atomic Energy Agency, Vienna, Austria.

Objective: In the scope of a prospective trial evaluating different Tc-99m radiopharmaceuticals for the diagnosis of breast cancer (IAEA E1.30.17) we investigated the value of 99mTc metilendiphosphonate (MDP) scintimammography in the assessment of palpable breast masses. Early MDP images have been advocated with a role in this subject.

Material and Methods: Seventy patients with palpable breast lumps referred from different centers from Chile, China, India, Peru, Tanzania and Turkey were studied with MDP and X-ray mammograms and then submitted to

BREAST	X-Ray Mammo	MDP
Sensitivity	88.9 % (C.I.: 77.4%-95.8%)	64.5% (C.I.: 51.3%-76.3%)
Specificity	72.2% (C.I.: 46.3%-90.3%)	40.0% (C.I.: 12.2%-73.8%)
LR positive	3.2 (1.7-7.1)	1.1 (0.7-2.1)
LR negative	0.1 (0.07-0.3)	0.9 (0.5-2.2)

Mammogram sensitivity was better than MDP (p:0.0024).

biopsy. Two patients had bilateral lesions. The group mean age corresponded to  $51 \pm 13$  yr with lesions ranging from 17-47mm. Prone lateral views and anterior supine scan were performed 10 min after MDP injection using an isotime acquisition of 10 min and a dose of 740 MBq. Axillary regions were evaluated in 36 cases. Two independent observers blinded for clinical data interpreted all scans. Positive scans were those with focal and well defined breast or axillary tracer uptake.

Results: Ten out of 72 breast lesions were benign and in 13/36 cases there was no malignant axillary involvement. Moderate diffuse bilateral breast uptake was observed frequently. Interobserver concordance was 89.3% for breast and 81.1% for axillary lesions. The diagnostic value and likelihood ratio (LR) for breast lesions (using 95% Confidence Interval or C.I.) were as follows:

For lymphatic involvement diagnosis, MDP sensitivity and specificity were 13.0% (C.I.:2.8%-33.6%) and 92.3% (C.I.: 64.0%-99.8%), respectively.

Conclusion: MDP scintimammography using early images is not an accurate method for detecting palpable breast lesions. Compared with X-Ray mammogram, its overall value is much lower.

## Nefrología

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### La Acuaporina 4 no es necesaria para concentrar la orina en riñón de *Octodon degus*.

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La acuaporina 4 (AQP-4) está en la membrana basolateral de las células principales del túbulo colector en los mamíferos, donde participa en el mecanismo de concentración de la orina transportando agua a través de dicha membrana, la que ha ingresado a la célula a través de la AQP-2 apical. *Octodon degus* es un roedor de hábitats áridos del norte de Chile y posee una alta capacidad para concentrar la orina.

La distribución de AQP-4 en riñón, estómago y cerebro de *degus* se estudió por inmunocitoquímica e inmunoblot en preparaciones de membranas de corteza y médula renal de *degus* y rata. Se utilizaron *degus* y ratas sometidos a un periodo de restricción en la ingesta de agua de 10 y 4 días, respectivamente. Se midió la osmolalidad urinaria a final del tratamiento.

Los estudios de inmunocitoquímica e inmunoblot mostraron que AQP-4 no se expresa en ningún segmento tubular del riñón de *degus*; en el riñón de rata, sin embargo. AQP-4 se localizó en la membrana basolateral de los túbulos colectores, hallazgo que fue corroborado en los estudios de inmunoblot. En ellos



se obtuvo una banda de 29 K Da exclusivamente en el de riñón de rata.

En el cerebro de degus. AQP-4 está presente en las células ependimales que revisten el acueducto cerebral y en neuronas del núcleo supraóptico e hipocampo. En el estómago, la AQP-4 se expresa en la membrana basolateral de las células parietales, las que también muestran inmunorreactividad para la isoforma  $\alpha$ -1 (gástrica) de la  $H^+$ ,  $K^+$ ATPasa. .

Estos resultados muestran que la AQP-4 no está presente en el riñón de degus y sugieren que este canal no es necesario en el mecanismo de concentración de la orina en esta especie. Similares resultados se han obtenido en otros roedores con alta capacidad de concentrar la orina.

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## Renal Aquaporins In the Degus, a Southamerican Desert Rodent

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The degu, a desert rodent of northern Chile, has a high urine concentrating ability (up to 5000 mOsm/L), that enables it to survive in areas with little supply of drinking water. We studied the distribution and regulation of known renal aquaporins (AQPs) 1, 2, 3, 4 and

8 by immunohistochemistry and immunoblotting in control, dehydrated and water loaded degus.

AQP-1 is expressed in proximal tubules, thin descending loops of Henle and vasa recta. In proximal tubules, AQP-1 colocalized with Na/Pi2 cotransporter. AQP-2 was found in cortical and medullary collecting duct cells that also express Na,K-ATPase. Compared to controls, dehydration produced a redistribution of immunoperoxidase labelling from cytosol to apical membrane without a significant increase in protein abundance; water loading markedly reduced AQP-2 immunolabeling and protein abundance. AQP-3 had a basolateral distribution in the same cells as AQP-2, it was affected in the same manner as AQP-2 by changes in water ingestion. Neither AQP-1, 2 or 3 colocalized with NKCC2 from thick ascending limbs of Henle.

AQP-4 immunolabelling was not detected in collecting ducts as in the rat, but it was expressed in gastric glands and brain areas.

AQP-8 had a intracellular distribution in proximal tubules and weak labeling was observed in collecting ducts. .

These results suggest a somewhat different regulation of AQP-2. AQP-4 is probably not necessary for urine concentration.

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## Alta incidencia de diarrea por *Clostridium difficile* en pacientes nefrológicos.

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En los últimos años han aumentado los casos de diarrea por *Clostridium difficile* (DCD) en pacientes nefrológicos, identificándose a la insuficiencia renal crónica (IRC) como factor de riesgo para su desarrollo. El objetivo del trabajo fue estudiar incidencia, forma de presentación y mortalidad de DCD en nefrópatas.

Se estudiaron retrospectivamente los casos que se presentaron desde Junio del 2000 a Mayo del 2001 en el Hospital Clínico Universidad de Chile. De las fichas se obtuvieron datos demográficos, forma de presentación, antibióticos asociados, respuesta al tratamiento y evolución. Se utilizó test de chi cuadrado con corrección de Yates para análisis estadístico.

Se pesquisaron 136 casos (incidencia 0.53/100 egresos); en nefrología hubo 48 episodios en 35 pacientes con una incidencia 7 casos/100 egresos ( $p < 0.001$ ).

Se tuvo acceso a ficha de 33 pacientes, 16 hombres y 17 mujeres, con edad promedio de 63 años. Diagnósticos de ingreso: IRC en hemodialisis 48%, síndrome urémico 36% y trasplante renal 6%, 26 pacientes (79%) tenían antecedente de uso de antibióticos, (42% ciprofloxacino y 34% alguna cefalosporina). En 3 pacientes el único factor de riesgo fue IRC. La diarrea se asoció a dolor abdominal en 27%, rectorragia en 1200 fiebre en 27% y megacolon tóxico en 1 caso.

En cuanto al tratamiento 75% respondió a metronidazol y 27% recayó siendo la recaída en los otros servicios de 6.3% ( $p < 0.02$ ).

Ocho pacientes (24%) fallecieron durante la hospitalización siendo la mortalidad del servicio en igual periodo de 5.7%. ( $p < 0.001$ ).

En conclusión la DCD es más frecuente, se asocia a mayor mortalidad y a mayor tasa de recaída en el servicio de nefrología que en otros servicios del hospital. El antibiótico que más se asoció fue ciprofloxacino y en el 9% la IRC fue el único factor de riesgo identificado.

Nefrología Latinoamericana 2002; 9: 101 (S159)

## Distribución y regulación de Acuaporinas en el riñón de *Octodon degus*.

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Las acuaporinas (AQP) son transportadores de agua fundamentales en la concentración y dilución urinaria. *Octodon degus* es un roedor de hábitats desérticos de Chile, dotado con alta capacidad para concentrar la orina. El objetivo de este trabajo fue caracterizar la distribución y regulación de las AQPs 1, 2 y 3 en el riñón de *O. degus*.

Se utilizaron machos adultos (200 g), separados en tres grupos: Control (libre ingesta de agua y alimento), restricción en la ingesta de agua (10 días sin agua, alimento ad libitum), sobrecarga acuosa (sacarosa 200% p/ v por 5 días como bebida). Se midieron las osmolalidades plasmática y urinaria al inicio y término del experimento para verificar el estado del balance hídrico. Se extrajeron ambos riñones y fueron procesa-

dos para inmunocitoquímica, inmunofluorescencia o preparación de membranas, usadas en los inmublots.

AQP-1 abunda en túbulos proximales contorneados y rectos, asas, delgadas descendentes y algunos capilares de la vasa recta. En túbulos proximales AQP-1 está en las membranas apical y basolateral. AQP-2 está en túbulos colectores corticales y medulares; la inmunorreactividad se localizó en las células principales. La deshidratación provocó una marcada redistribución a la membrana apical, más que un aumento en la abundancia: la sobrecarga acuosa redujo remarcadamente su abundancia.

AQP-3 está en la membrana basolateral de las mismas células que, expresan AQP-2. La deshidratación aumentó levemente y la sobrecarga acuosa redujo drásticamente su abundancia.

Estos resultados sugieren un modo diferente de regulación de las AQP-2

y 3 en el riñón de esta especie de hábitats desérticos.

Financiamiento Fondecyt N° 2990008. a P. Gallardo.

## **Neumología**

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*Eur Respir J 2002; 20:1490-8*

### **Effects of noninvasive ventilation on lung hyperinflation in stable hypercapnic COPD.**

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Two previous uncontrolled studies have suggested that noninvasive mechanical ventilation (NIMV) in patients with hypercapnic chronic obstructive pulmonary disease (COPD) improves arterial blood gas tensions by decreasing lung hyperinflation with the consequent reduction in inspiratory loads and changes in ventilatory pattern. The aim of this randomised placebo-controlled study was to determine whether these mechanisms play a pivotal role in the effects of NIMV on arterial blood gases. Thirty-six stable hypercapnic COPD patients were randomly allocated to NIMV or sham NIMV. A 2-week run-in period was followed by a 3-week study period, during which ventilation was applied 3 h x day<sup>-1</sup>, 5 days a week. Arterial blood gases, spirometry, lung volumes, and respiratory mechanics were measured before and after application of NIMV. Patients submitted to NIMV showed changes (mean (95% confidence interval)) in daytime arterial carbon dioxide tension (Pa,CO<sub>2</sub>) and arterial oxygen tension of -1.12 (-1.52-0.73) kPa (-8.4 (-11.4-5.5) mmHg) and 1.14 (0.70-1.50) kPa (8.6 (5.3-11.9) mmHg), respectively. Total lung capacity, functional residual capacity (FRC) and residual volume were found to be reduced by 10 (7-13), 25 (18-31), and 36 (27-45)% of their predicted

value, respectively, whereas forced expiratory volume in one second and forced vital capacity increased by 4 (1.5-6.9) and 9 (5-13)% pred, respectively. Tidal volume (VT) increased by 181 (110-252) mL. All of the above changes were significant compared with sham NIMV. Changes in Pa,CO<sub>2</sub> were significantly related to changes in dynamic intrinsic positive end-expiratory pressure, inspiratory lung impedance, VT and FRC. It was concluded that the beneficial effects of noninvasive mechanical ventilation could be explained by a reduction in lung hyperinflation and inspiratory loads.

## **Neurología-Neurocirugía**

2002 European Sleep Research Society, *JRS* 11 (1), 1-260

# Sleep regulation in the rat exposed to changes in ambient temperature

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**Keywords:** REM sleep deprivation, REM sleep rebound, low ambient temperature, Delta power density

**Objetives:** The exposure to low ambient temperature (Ta) represents and homeostatic challenge which induces a sleep deprivation, followed by a sleep rebound during the subsequent recovery period at normal laboratory Ta <sup>(1)</sup>. In previous studies, which were carried out in the rat without a full characterization of sleep occurrence in the cold, it was

shown that the rebound of REM, sleep (REMS) consisted in an increase in the amount of REMS, broadly proportional to the degree of REMS <sup>(2)</sup>, whilst non-REM sleep (NREMS) rebound was mainly characterized by an increase in the EEG power density in the Delta (0.75-4 Hz) band <sup>(3)</sup>. The present study was carried out to clarify the quantitative aspects of sleep regulation under the influences of a wide range of low T<sub>a</sub>.

**Methods:** Twenty-four male Sprague-Dawley rats (250g, acclimated to 24 ± 0.5°C and to 12:12h (L:D) cycle (09.00-21.00 L) carrying electrodes for EEG recording, were used. Following 2 days of baseline recording, animals were exposed for 24 h to T<sub>a</sub>s ranging from 10 to 10°C and subsequently allowed to recover by returning to a T<sub>a</sub> of 24°C.

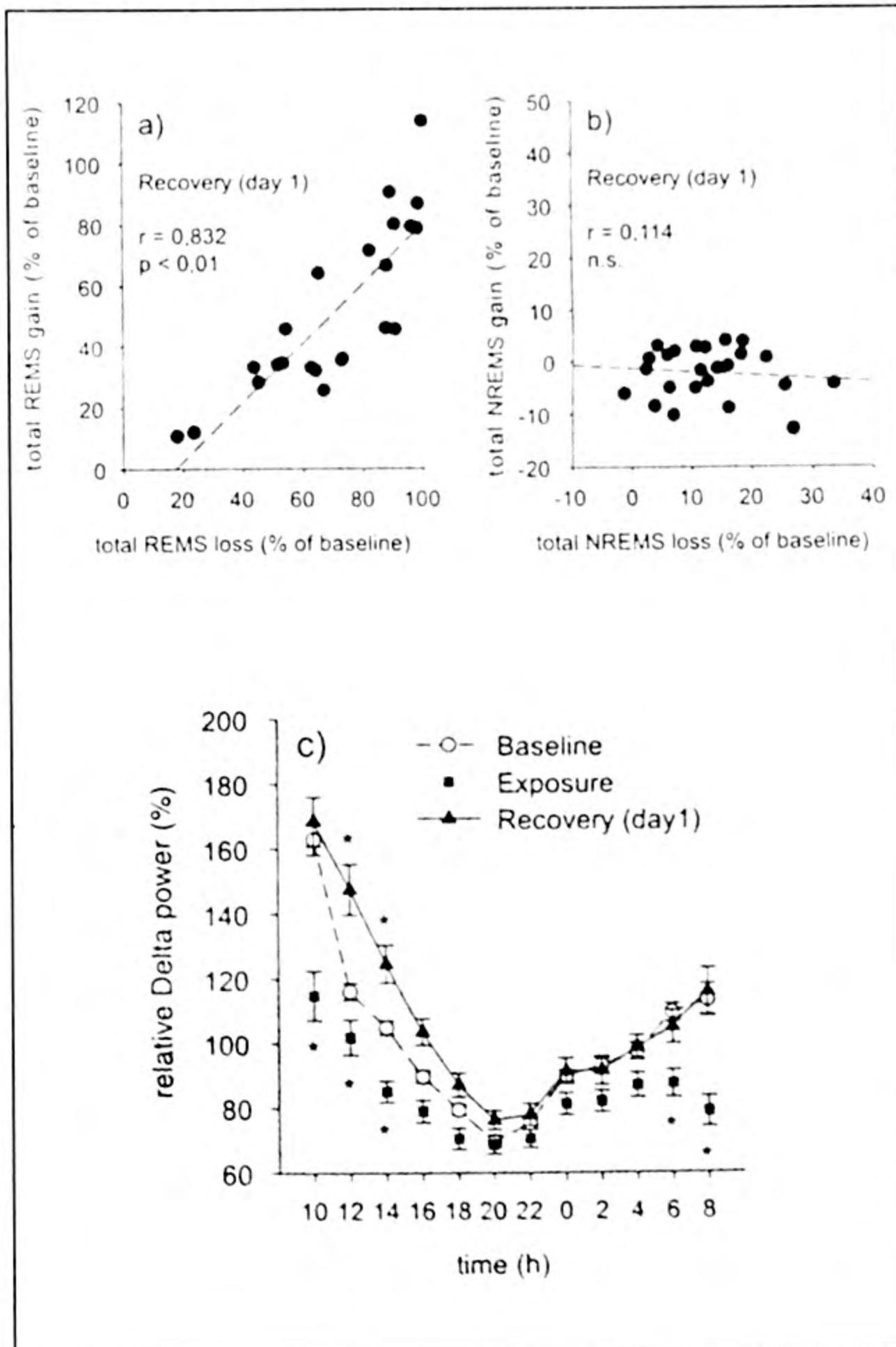
**Results:** For each animal, the relationship between the amount of either REMS(a) or NREMS, (b) loss at low T<sub>a</sub> and the amount gained during the first 24-h recovery period, is shown (100%, 24-h baseline amount: dashed line, linear regression). The results show that the correlation between the experimental variables was significant for REMS but not for NREMS. However, the analysis of the time course of EEG power density in the Delta (0.75-4 Hz) band in NREMS (c; mean ± SEM; 100%, average 24-h baseline levels) show that, with respect to baseline, Delta power was depressed across the 24-h period of exposure to low T<sub>a</sub> and enhanced during the early recovery period (ANOVA:\*, P<0.05). The results are summarised in the figure.

**Conclusions:** Our experimental conditions allows a clearcut distinction in the expression of mechanism underlying sleep regulation, i.e. a close control of the amount for REMS, but not for NREMS, and a modulation of the time course of Delta power density for NREMS. The amount of REM sleep is closely controlled in

## Short-term homeostasis of REM sleep assessed in an intermittent REM sleep deprivation protocol in the rat.

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the rat exposed to changes in ambient temperature.

An intermittent rapid eye movement (REM) sleep deprivation protocol was applied to determine whether an increase in REM sleep propensity occurs throughout an interval without REM sleep comparable with the spontaneous sleep cycle of the rat. Seven chronically implanted rats under a 12 : 12 light-dark schedule were subjected to an intermittent REM sleep deprivation protocol that started at hour 6 after lights-on and lasted for 3 h. It consisted of six instances of a 10-min REM sleep permission window alternating with a 20-min REM sleep deprivation window. REM sleep increased throughout the protocol, so that total REM sleep in the two REM sleep permission windows of the third hour became comparable with that expected in the corresponding baseline hour. Attempted REM sleep transitions were already increased in the second deprivation window. Attempted transitions to REM sleep were more frequent in the second than in the first half of any 20-min deprivation window. From one deprivation window to the next, transitions to REM sleep changed in correspondence to the amount of REM sleep in the permission window in-between. Our results suggest that: (i) REM sleep pressure increases throughout a time segment similar in duration to a spontaneous interval without

REM sleep; (ii) it diminishes during REM sleep occurrence; and (iii) that drop is proportional to the intervening amount of REM sleep. These results are consistent with a homeostatic REM sleep regulatory mechanism that operates in the time scale of spontaneous sleep cycle.

2002 European Sleep Research Society JSR, 11 (S1) 163

## REM sleep rebound after total or selective rem sleep deprivation assessed in an intermittent rem sleep deprivation protocol in the rat

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**Keyword:** REM sleep homeostasis. REM sleep deprivation, total sleep deprivation

**Objectives:** In a previous work <sup>(1)</sup>, by combining total sleep deprivation (TSD) with selective REM sleep deprivation (RSD) we showed that both the build up of pressure to enter REM sleep and the REM sleep rebound depend on the time elapsed without REM sleep, regardless of the presence of the NREM sleep allowed during deprivation. We designed an intermittent REM sleep deprivation protocol (IRD) consisting of alternating short windows of selective REM sleep deprivation and spontaneous sleep (see Methods), to measure REM

sleep rebound in parallel with the temporal course of REM sleep pressure build up [2]. The aim of the present work is to compare the time courses of REM sleep rebound after 2 h of TSD or RSD followed by an intermittent REM sleep deprivation schedule.

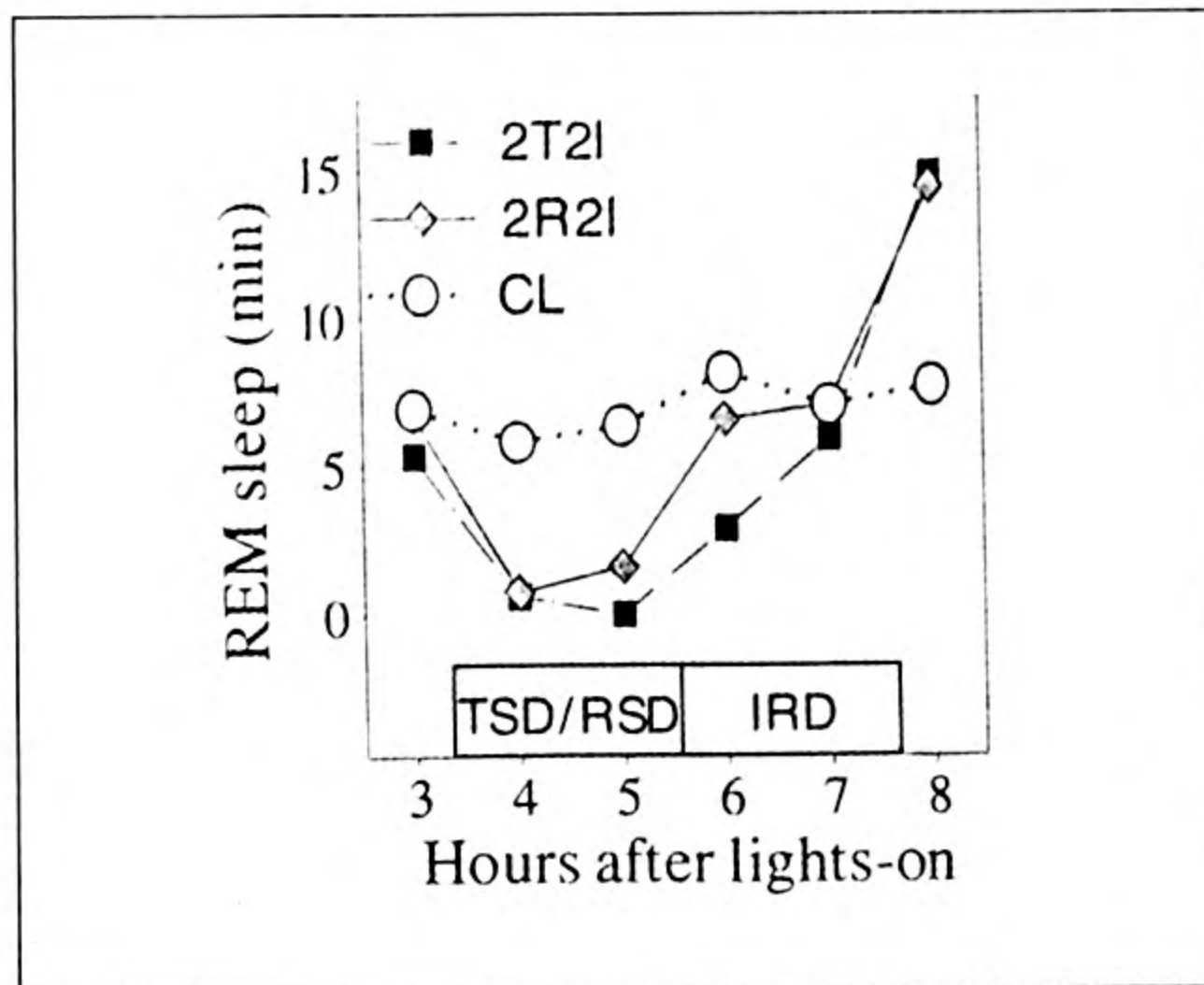
**Methods:** Five adult male Sprague-Dawley rats were chronically implanted and maintained under a 12 : 12 LD schedule in individual isolation chambers. A real-time acquisition system sampled (at 250 Hz), stored and displayed polygraphic signals. Visual state scoring (wakefulness, NREM sleep or REM sleep) was performed with a time resolution of 15 s. After two baseline days each rat was subjected to two protocols starting with: (a) 2T21 protocol:

2 h TSD followed by 2 h of IRD; the following protocol was (b) 2R21 protocol: 2 h of RSD followed by 2 h of IRD. IRD consisted in the alternation, for four successive times, of 10 min of spontaneous sleep (REM sleep permission window), and 20 min of selective REM sleep deprivation (REM sleep deprivation window). Finally, a control (CL) session, that matched interventions during 2R21, was also run. Protocols and control sessions were started at hour 4 after lights-on. One recovery day was left between trials. ANOVA for factors protocol and hour, and paired *t*-tests were applied.

**Results:** During TSD (hours 4 and 5, protocol 2T21) REM sleep suppression was almost total. During RSD (hours 4 and 5, protocol 2R21) REM fell under 10% of baseline. During the first hour of IRD (hour 6 after lights on), REM sleep expression in 2T21 was significantly lower than in the CL condition, whereas in 2R21, REM sleep expression did not differ from CL or baseline. At hour 8 after lights-on (first hour of recovery) both 2T21 and 2R21 showed a REM sleep rebound that more than doubled baseline and CL (see Figure, baseline data

not shown). In 2R2I, the fraction REM/Total sleep time in REM permission windows is higher respect to CL already at hour 6, whereas REM/total sleep time in REM permission windows during hour 6 is lower for 2T2I respect to CL and 2R2I. REM sleep rebound begins earlier after selective REM sleep deprivation than after total sleep.

Acknowledgements: Parts of this research was supported by grants FONDECYT 3010028 (A.O.) and 1990631. E Brunetti is a Doctoral Fellow of the Instituto de Ciencias Biomédicas (ICBM).



## Wheel running does not change phase preference of rest-activity rhythm in a nocturnal octodontid

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Keywords: circadian rhythms, wheel running, non-photic entrainment, octodon bridgesi, octodon degus

Objectives: It has been described that wheel-running (a non-photic stimulus) produces a rapid diurnal-nocturnal inversion in phase preference in *Octodon degus* (RODENTIA: HYSTRICOGNATHI). This phenomenon occurs in entrained and free-running individuals that exhibit a diurnal chronotype [1]. *Octodon degus* is a crepuscular semi-fossorial species, that inhabits xeric habitats of central Chile.

Under controlled conditions, *Octodon bridgesi* (Waterhouse, 1844), a close relative of *O. degus* [2] that lives in the temperate forest of centre-south Chile, expressed a nocturnal phase preference in the restactivity rhythm without crepuscular activity bouts [3]. Here, we describe the effect of wheel-running exposure on rest activity rhythm in *O. Bridgesi*.

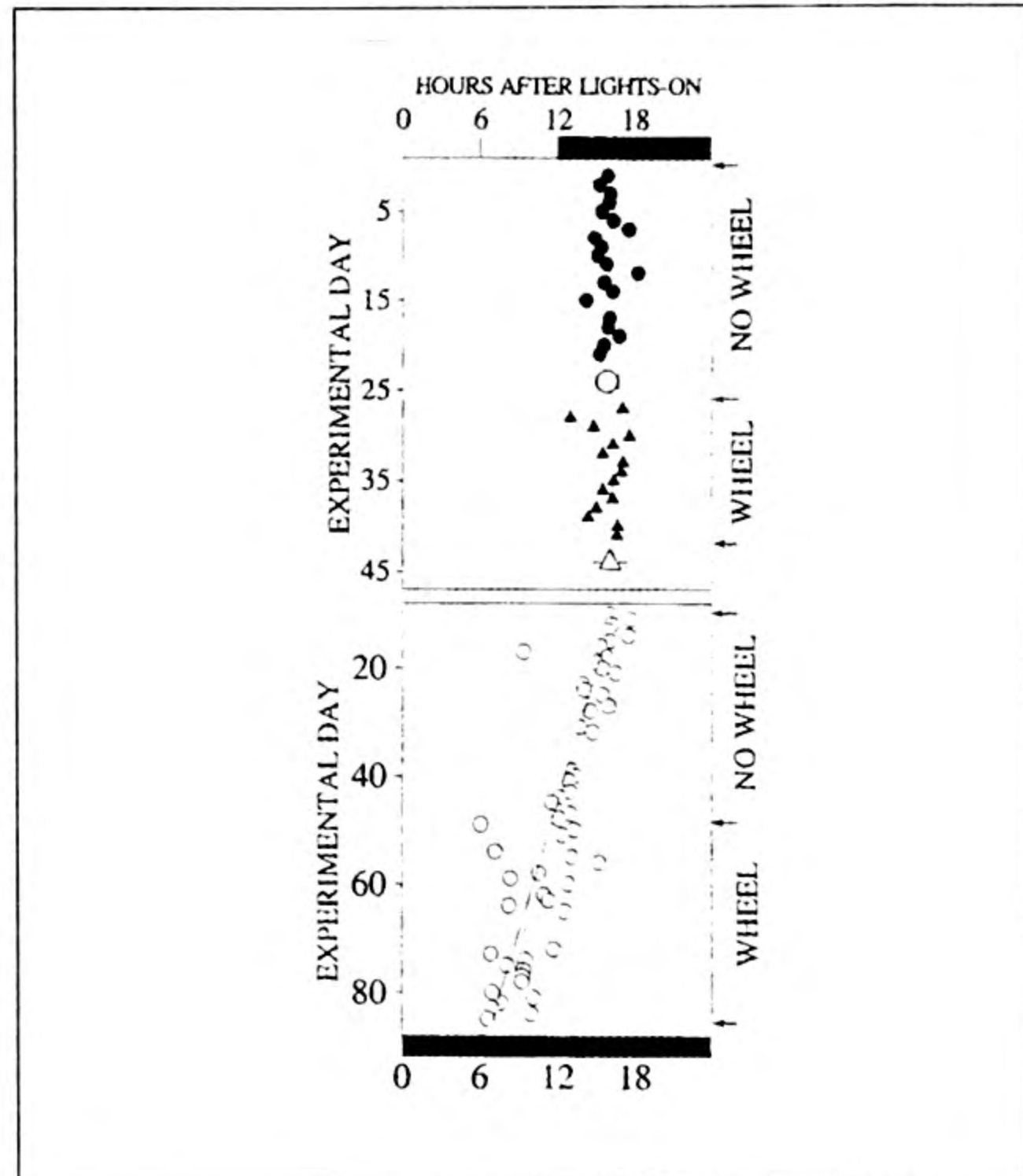
Methods: Two male adult *O. bridgesi*, were captured in the field and installed in cages (30 x 40 x 30 cm) contained in individual isolation chambers (65 x 60 x 60 cm), under a 12: 12 light-dark schedule (3001x) and at 23°C, with food and water *ad libitum*. A runningwell

was inside the cage, that could be locked or unlocked (NO WHEEL condition, respectively). An Automated acquisition system recorded

and store with a 15-s resolution the activity detected by a movement trasducer placed at the base of the animal's cage. After a period of adaptation, each animal was subjected to four conditions (A) entrained to a 12 : 12 LD schedule with running-wheel locked (LD-NO WHEEL condition); (B) entrained with unlocked running-wheel (LD-WHEEL condition); (C) free-running (constant darkness, DD) with running-wheel locked (DD-NO WHEEL condition), and (D) free-running with unlocked running-wheel (DD-WHEEL condition). Angular statistics (cosinor rhythmometry) were applied four hourly incidence of 15-s bins with the highest 20% activity events. Acrophases (mean angles) are expressed in hour respects to lights-on (zeitgeber-time).

Results: Figure 1 depicts acrophases of 22 consecutive days under LD-NO WHEEL condition (filled circles) followed by 16 days under LD- WHEEL condition (filled-triangles). The animal concentrates the activity phase during the objective night with means at hour  $15.8 \pm 0.9$  and  $16.1 \pm 1.3$  in LD-NO WHEEL (open circle + SD) and LD- WHEEL (open triangle + SD), respectively. It was found a reduction in rest-activity rhythm amplitude under LD-WHEEL condition. During free running, it was observed a period shorter than 24 h in the who individuals studied. Figure 2 show acrophases (open circles) of one of the animals maintained in constant darkness. After 44 days in DD-NO WHEEL, the animal is exposed to DD-WHEEL condition. After a transient interval of high variability, acrophases in DD-WHEEL condition tend to fall at the phase predicted (line  $t = 23.87$ ) from the acrophases obtained during DD-NO WHEEL period (days 1-44).

Discussion: *O. Bridges* and *O. Dardgus* being phylogenetically close relatives, evolved under ecological pressures that determined



different chronobiological strategies. *Octodon* emerges as a Genus of high interest for comparative chronobiological studies. Wheel-running does not change phase preference nor rest-activity rhythm period in *Octodon bridgesi*.

Acknowledgements: Research supported by grant FONDECYT 3010028. Thanks are due to Drs Rodrigo Vásquez, Bárbara Saavedra and Ennio vivaldi.



# Short-Term REM sleep homeostasis and rem sleep triggering by the light to dark transition.

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**Keywords:** REM sleep homeostasis, light, REM sleep induction, REM sleep regulation.

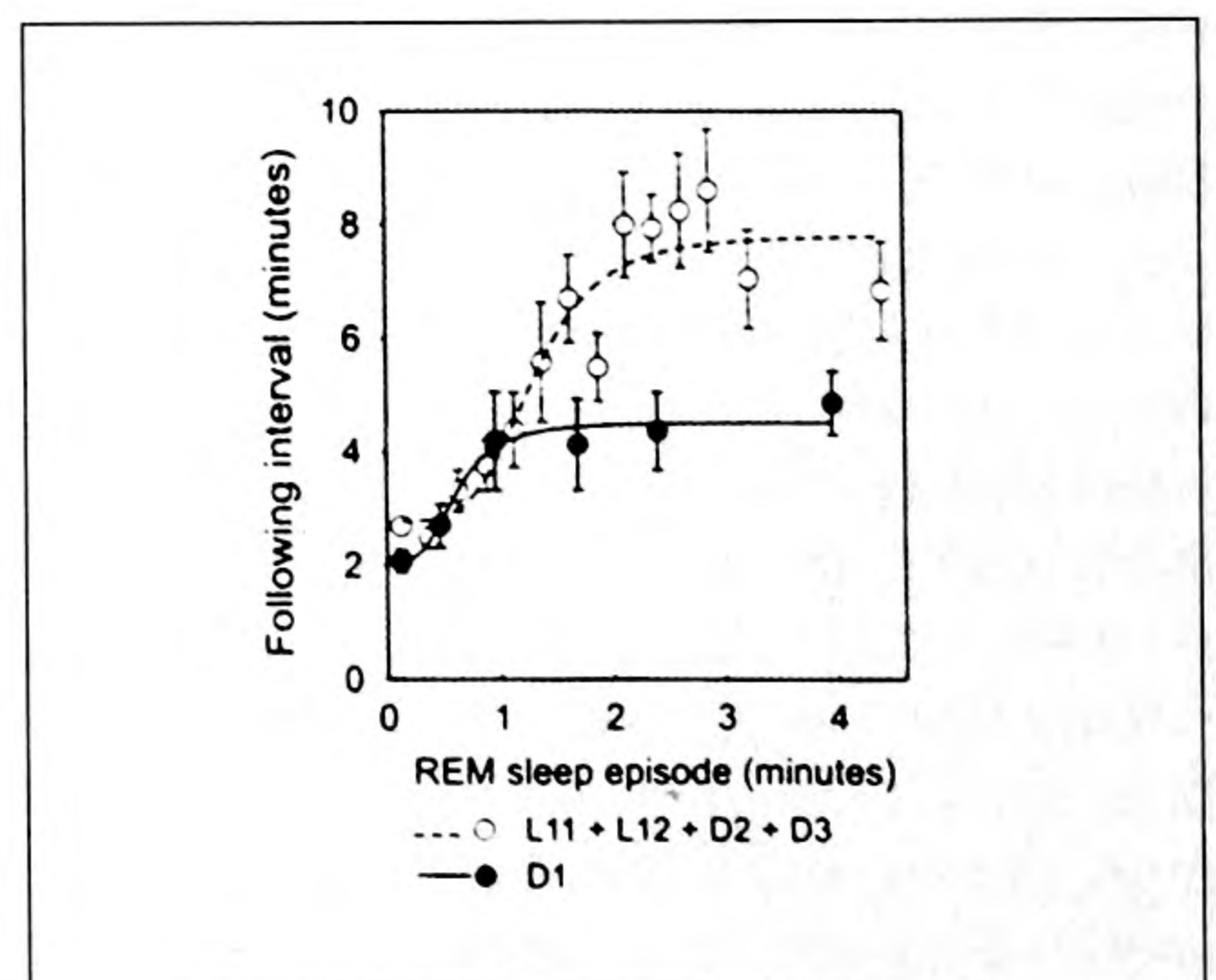
**Objectives:** There is a short-term homeostatic regulatory mechanism that relates the duration of a given REM sleep episode to the duration of the following interval up to the next REM sleep occurrence (1).

There is a modulation of this short-term homeostasis when assessed at different phases of a 12:12 L:D cycle, reflecting the circadian control of REM sleep. Light has a direct effect on REM sleep, its expression being enhanced or inhibited when lights are turned off and on, respectively (2). In this report we evaluate how lights-off affect short-term REM sleep homeostasis. We assess short-term REM sleep homeostasis in the eyes from the first hour of darkness and compare in with those from the 4 h that surround it, and hence do not differ much in circadian phases.

**Methods:** Sixteen adult male Sprague-Dawley rats chronically implanted for EEG and EMG recording and maintained under a 12:12 LD schedule. An automated system detected delta, sigma and theta activities and EMG spike, and stored their incidence in 15-s

epochs for off-line state scoring. Duration of REM sleep episodes and intervals were determined (intervals had to have a 2-epoch duration). One episode and its following interval constituted a cycle. Two pools were made, one with the cycles from the first hour of darkness (D1), and the other with the cycles from the last 2 h of light (L 11 and L 12) and the second and third hours of darkness (D2 and D3). The first pool contained 271 cycles and the second pool 1030. Robust means and standard errors were obtained for the set of intervals that followed episodes of a given duration (episode duration categories could be grouped so that robust means were always from at least 30 observations) (3)

**Results:** The figure displays the robust means and standard errors of the L11 + L12 + D1 + D2 and of the D1 pools (Figura 1). Each set of data can be fitted into a logistic equation of type  $y = y_0 + a / (1 + (x/x_0)^b)$ . The estimated amplitude parameter 'a' in the equation) is significantly different between both curves. Visual inspection evidences the similarity of interval duration in both pools up to a REM episode duration of 1.13 min, i.e. the lower limit and initial rising phase of both curves. At



that point the D1 curve reaches its plateau, whereas the curve of the four adjacent hours goes on incrementing to reach its upper limit at REM episode duration of 2.13 min.

**Conclusions:** The direct effect of lights-off in triggering REM sleep can be assessed as a change in the short term homeostatic regulatory mechanism. This change results in longer REM episodes being less effective in pushing further away the transition into the next REM episode. The direct effect of lights-off in the triggering REM sleep involves a change in short-term REM sleep homeostasis.

**Acknowledgement:** Supported by grant FONDECYT 1990631.

## **Obstetricia y Ginecología**

*Fertil Steril 2002;78 :90-5*

### Mean versus individual hormonal profiles in the menstrual cycle.

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**Objective:** To evaluate hormonal profiles of normal menstrual cycles. **Design:** Prospective, descriptive study of a case series. **SETTING:** University-based natural family planning center. **PATIENT(S):** Twenty-five natural family planning users for three or more cycles (n = 78). These women were healthy, contraception-free, parous, with regular ovulatory cycles. **INTERVENTION(S):** Immunoassays for estrone glucuronide, LH, and pregnanediol glucuronide were done in daily timed and measured samples of early morning urine. **MAIN OUTCOME MEASURE(S):** Estrone glucuronide, LH, and pregnanediol glucuronide levels were measured during the menstrual cycle. **RESULT(S):** All cycles showed an ovulatory pattern configuring classic hormonal mean curves. Most (77%) differed from the mean curve pattern. All had estrone glucuronide peaks, LH peaks, and pregnanediol glucuronide increases. Estrone glucuronide and LH peaks were not always clear; some lasted more than 1 day (long peak: estrone glucuronide 19%, LH 9%) or fluctuated (double peak: estrone glucuronide 4%, LH 6%; small LH peak: 19%). There were also prepeak estrone glucuronide surges, and pre- and postpeak LH surges. Pregnanediol glucuronide increased more clearly (6% fluctuated 1 day). Some wo-

men had repeated cycles with long estrone glucuronide peaks (16%) and fluctuations in LH surge (44%). Conclusion(s): Normal menstrual cycle hormonal profiles generally differ from mean curves, which are usually considered standard.

*Ultrasound in Obstetrics & Gynecology 2002; 20: 50-1*

## Circumvallate Placenta and Fetal Growth Restriction.

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Circumvallate placenta infrequently occurs and may be associated with increased perinatal morbidity. The objective is to communicate two cases of severe Fetal Growth Restriction (FGR) during mid-trimester in two apparently healthy pregnant women with circumvallate placentas diagnosed by pathologist.

Both patients had no maternal disease (hypertensive, infectious or immunological) and presented on week 28 with severe intrauterine FGR, under 5th percentile (600 and 590 grams, Hadlock). The doppler ultrasound showed bilateral augmented resistance and notch in the maternal uterine artery. Both fetus had absent diastolic flow in the umbilical artery, diminished resistance in middle cerebral artery, and normal waveform in ductus venosus. Amniotic fluid, biophysical profile, FHR trace and cariotype were normal. Medical management with tightened vigilance was intended for eleven days and we persistently observed the hemodynamical changes of arterial redistribution and normal venous flow pattern as described. After this period, cesarean section was done and the new born

(780 gr, Apgar 8-9 and 650 gr, Apgar 4 -8), had a good evolution.

Placental pathology revealed extracorialis circumvallate, 160 gr and intervillous space thrombosis each.

Conclusion: 1. Placenta circumvallate was associated with severe restriction fetal growth and both cases had a latency period with fetus able to maintain compensatory mechanism, before the interruption.

2. Second trimester, severe FGR in apparently healthy women orient to suspect diagnosis and it requires detailed antenatal placental scan.

*BJOG 2002; 109: 297-301*

## Levels of C-reactive protein in pregnant women who subsequently develop pre-eclampsia.

Savvidou MD, Lees CC, Parra M, Hingorani AD, Nicolaides KH.

Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, UK.

Objective: To investigate whether a maternal inflammatory response precedes the development of preeclampsia. DESIGN: Cross-sectional study. Setting: Antenatal clinic in an inner city teaching hospital. Population: Two groups of women were examined at 23-25 weeks of gestation. The first group (45 women) had normal uterine artery Doppler waveforms and subsequently had a normal pregnancy outcome. The second group (45 women) had Doppler evidence of impaired placental perfusion and 21 (47%) of them had normal outcome, 14 (31%) developed intrauterine growth restriction and 10 (22%) developed

pre-eclampsia, with or without intrauterine growth restriction. METHODS: C-reactive protein, an acute-phase reactant, was measured in maternal serum using a highly sensitive method with a detection limit of 0.05 mg/L. MAIN OUTCOME MEASURES: Development of pre-eclampsia, as defined by the International Society for the Study of Hypertension in Pregnancy. Intrauterine growth restriction was defined as birthweight <5th centile for gestation and sex of the neonate. Results: The serum C-reactive protein concentration in women who subsequently developed pre-eclampsia (median 1.56, range 0.55-3.12 mg/L) or delivered a baby with birthweight <5th centile (median 0.74, range 0.64-1.58 mg/L) was not significantly different from that in women with uncomplicated pregnancies (median 1.28, range 0.75-2.08 mg/L;  $P = 0.95$  and  $P = 0.62$ , respectively). Conclusion: These findings suggest that the onset of clinical signs of pre-eclampsia may not be preceded by a maternal inflammatory response, as assessed by measurement of C-reactive protein.

*Crit Rev Oncol Hematol 2002; 41:335-41*

## Secondary cytoreductive surgery in the patient with recurrent ovarian cancer is often beneficial.

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The majority of women with ovarian cancer will present at an advanced stage and ultimately

experience a recrudescence of tumor. Recent data indicates that secondary cytoreductive surgery is feasible, well tolerated and associated with significant prolongation of survival in selected patients with recurrent ovarian cancer.

*Yonsei Med J 2002; 43: 754-62*

## Surgical management of recurrent cervical cancer.

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The majority of patients with recurrent cervical cancer are incurable and treatment is based on the type of primary therapy delivered. Only a very small percentage of the patients with recurrent cervical cancer following primary radiotherapy will have central pelvic recurrences that are amenable to surgical resection and curable by pelvic exenteration. These procedures should be undertaken only after the completion of exhaustive attempts to exclude extrapelvic disease.

3rd World congress of pediatric Infectious diseases-  
WSPID

Santiago, Chile, November 19-23, 2002; 06-1S8

### Distinctive humoral immune response to protein fractions of stec in hemolytic uremic syndrome patients.

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Post-enteropathic Hemolytic Uremic Syndrome (HUS), is the most frequent cause of acute renal failure in infants and children around the world. Evidences have shown the protagonic role of Shiga-toxin producing E. coli (STEC) infection in HUS. The immune response against STEC is not completely understood. Aim. To study markers of the humoral immune response against STEC infection of value to predict extraintestinal complications like HUS. Methods. 30 HUS patients and 30 age matched children with diarrhea were included; paired serum samples were obtained and immune response was studied by immunoblot to 3 different protein fractions (outer membrane, cytoplasmatic membrane and cytoplasmic proteins). Protein fractions were purified from STEC isolates serogroups 0157, 026 and 0111. Results. The recognition of outer membrane and cytoplasmatic proteins was similar in serum samples from HUS patients and controls, but a distinct response against a cytoplasmic membrane protein, (CMP), 60-90-kDa, was observed in HUS patients more frequently than in controls.  $p < 0.0001$ . Median of antibody titers against

the 0157 CMP fraction was 1: 5.000 in controls and 10 fold higher, 1: 50.000 in HUS patients. Moreover, 9 out of 30 HUS patients seroconverted (increased antibody titers 2 to 10 times). Conclusions. The recognition of CMP fractions by HUS patients may represent a marker suggesting systemic complications in STEC infected patients. FONDECYT No 1000636

*Acta Pediatr* 2002; 91: 430-3

### Continuous gastric drip versus intravenous fluids in low birthweight infants

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Continuous gastric drip versus intravenous fluids in low birthweight infants. *Acta Pediatr* 2002; 91: 430-433. Stockholm. ISSN 0803-5253

This multicentre randomized study compared a continuous gastric drip (CGD) with intravenous (i.v.) fluid administration. Healthy newborns with birthweight from 1501 to 2000 g whose physician ordered i.v. fluids were randomized before the 2nd hour of life to CGD or i.v. fluids. The major outcome variable was the need for an i.v. line in the CGD group. Serum glucose was measured at 30 min, 1 h and every 6 h thereafter. Serum sodium and potassium were measured at least once during the first 72 h of life. Enteral feedings, feeding intolerance, number of venous lines and i.v. line-related complications were recorded until the interruption of CGD or the i.v. line. Twenty-nine infants were randomized to each group. The two groups were comparable in terms of birthweight and gestational

age. Ten percent (3/29) of the infants randomized to the CGD group required i. v. fluids and 90% of them received electrolytes and glucose through an orogastric tube. The incidence of hypoglycaemia, hyponatraemia and episodes of feeding intolerance did not differ between the groups.

Conclusion: Fluid administration by CGD reduces the need for i.v. lines without increasing the risk of complications.

Key words: Continuous gastric drip, intravenous line, low birthweight infant, neonatal intensive care unit.

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53 (S)

## Prevalence of intestinal parasites in oncological patients and healthy children

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Intestinal parasites are prevalent in Chilean children. They have frequencies between 10-90% There are not reports related to parasitic prevalence in patients with oncological pathology without diarrhea.

Aims: To determinate the parasitic frequency in oncologic patients and to compare the same frequency in healthy children. To investigate in both groups the presence of traditional intestinal parasites (Burrows method). Ziel

Neelsen stain method for *Cryptosporidium* spp. *Cyclospora* spp. and *Microsporidium* (Chromotrope 2 R technic) A prospective study was performed in 32 children with oncological pathology and chemotherapy and in 90 healthy children (same ages). Only patients without diarrhea episodes were included in both groups.

Results: Common intestinal parasites were found 6.3% and 22% in oncological patients and healthy groups respectively. The most frequent parasites were *B. hominis* (6.9%) and *G. lamblia* (8.1%) in healthy group; instead in oncological patients both parasites had a frequency of 3.2% *Cryptosporidium* spp and *Cyclospora* were not found. An important outcome was the higher frequency of *Microsporidium* (18%) in the oncological pathology group than in healthy group (4%)  $P < 0.05$  The frequency of common parasites was higher in healthy children than in oncological group. (Relative risk of 0.28). Instead the higher prevalence of *Microsporidium* in Oncological patients should be considered, because of is an opportunistic agent that produced severe diarrhea in immunosuppressed. We recommend to study this agent in all the immunosuppressed patient receiving chemotherapy.

## Psiquiatría

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*Rev Panam Salud Publica 2002; 11: 430-4*

### Information, communication, and equity: dilemmas in health

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Equity, which is a form of justice, is the absence of inequalities that are evitable or unjust or that stem from preventable causes. In the area of health, it is linked to prudence that should prevail in the exercise of the health professions. Information, like any other social commodity, can be distributed in an inequitable way among different groups or populations due to technological barriers or cultural factors. However, knowledge is not just information; it is information that is aimed at a specific social purpose. Inequity in knowledge can be reduced by means of genuine communication, as Habermas proposed. This article deals with scientific communication as much as it does with public knowledge and the way information is disseminated.

## Psiquiatría - Medicina Nuclear

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*Rev Esp Med Nucl 2002; 21: 410-6*

### Behavior of brain perfusion with SPECT tomography 99mTc ethylene dicysteine (ECD) in alcohol and cocaine dependents during abstinence

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Brain perfusion abnormalities after an abstinence period of 28 days in a group of patients with alcohol and / or cocaine dependence was investigated. They were related with gender, consumption period and number of drugs. Fifty men and 10 women were included and SPECT perfusion was performed using 99mTc ethylene cysteine dimer (ECD) with qualitative and semiquantitative section analysis. Perfusion abnormalities were observed in 60% of the patients, principally in frontal, temporal and parietal lobes. The abnormalities were focal in 58.3%, diffuse in 41.7% and bilateral in 95% of all patients. Abnormalities were observed in 68% of the men and in only 20% of the women ( $p = 0.01$ ). Patients with brain perfusion abnormalities had a longer period of consumption corresponding to a median of 17.5 years in patients with abnormalities versus nine years in those with no abnormalities ( $p = 0.036$ ),

however, their ages as well as the number of drugs consumed were not significantly different. In conclusion, after 28 days of alcohol and / or cocaine abstinence there is significant presence of brain perfusion abnormalities with  $^{99m}\text{Tc}$  ECD. This could be explained by vasospasm and / or secondary endothelial lesions.

## **Psiquiatría - Obstetricia y Ginecología**

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*Revista Internacional Psiquiatría y Salud Integral 2002;*  
1: 61-67

### **Depresión postparto: alta frecuencia en puérperas chilenas, detección precoz, seguimiento y factores de riesgo.**

Dr. Luis Risco, Dr. Enrique Jadresic, Dra. Tamara Galleguillos, Dr. José Luis Garay, Dr. Marco González, y Dr. Jorge Hasbun.

#### **Postpartum Depression: High Rates in Chilean Women, Early Detection, Follow-up and Risk Factors**

Postpartum depression is a common disorder that has important short-and long-term consequences for mother and child. The objectives for this study were: to determine the presence of depressive symptomatology at day 3 and week 12 postpartum, to study the use of different psychometric scales for the early detection of postpartum depression, and to detect risk factors linked to postpartum depressive symptomatology. The prospective study was done between January and April, 1998. One hundred and three women at two

hospitals in Santiago, Chile, were assessed at day 3 postpartum using a specially devised file for sociodemographic data, the Graffar scale, the Hamilton scale for depression (HAM-D) and the Edinburgh Postnatal Depression Scale (EPDS). Forty-three of the women could be followed up and the scales for depression administered again at 12 weeks. For the sample of 103 women the rate for depressive symptomatology at day 3 was 6,8% with the HAM-D and 27,2% with the EPDS. For the subsample of 43 women the rate for depressive symptoms at day 3 was 4,6% with the HAM-D and 19% applying the EPDS; at 12 weeks the rates had raised to 27,9% and 48%, respectively. The rate for new cases of postpartum depressive symptomatology at week 12 was 23,2% according to the HAM-D and 32,5% according to the EPDS. The following factors were significantly associated with postpartum depressive symptoms: unwanted pregnancy, three or more previous children, living with no partner, normal delivery, marital conflicts, and being single. The EPDS, applied at day 3 postpartum, appeared as a predictor of depressive symptomatology at week 12 postpartum.



## **Radiología**

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*Pediatr Radiol 2002; 32: 485-91*

### **Sonographic diagnosis of acute spermatic cord torsion. Rotation of the cord: a key to the diagnosis.**

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**Background:** Although the primary abnormality in testicular torsion is at the spermatic cord, imaging studies up to now have mostly been oriented to evaluation of the testicle itself, with emphasis on color Doppler ultrasonography (US). However, findings can be inaccurate when there is incomplete interruption of testicular flow. Indirect findings, such as morphological changes in the testis alone, are not reliable for the diagnosis since they become evident late in the disease. **Objective:** To call to attention to the fact that sonographic visualization of the spermatic cord can be the key for diagnosis in those patients with acute scrotal pain as a result of testicular torsion, particularly when color Doppler US shows that intratesticular flow is present within the affected testis. **Patients and methods:** Six patients who presented clinically with acute scrotal pain and had spermatic cord torsion, proven at surgery. All patients were initially studied with color Doppler US, and intratesticular flow was detected in all of them. Patients who showed structural abnormalities on gray-scale US and/or absence of intratesticular vascular flow in the affected testis were not included. In addition to a conventional study, the spermatic cord was

examined. **RESULTS:** The spermatic cord was shown to be rotated on the symptomatic side in all patients. Local morphological and vascular flow changes, distal and at the site of the torsion, were found and registered. **Conclusions:** The finding of a rotated spermatic cord could be a highly reliable and direct sign for the diagnosis of a testicular torsion, and this is especially important when vascular flow is present within the affected testis on color Doppler US examination. Examination of the spermatic cord should be added to evaluation of the testis in patients with suspected testicular torsion to enhance sensitivity of the examination.

## **Reumatología**

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*Clin Diagn Lab Immunol 2002; 9: 1253-9*

### **Streptokinase promotes development of dipeptidyl peptidase IV (CD26) autoantibodies after fibrinolytic therapy in myocardial infarction patients.**

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Dipeptidyl peptidase IV (DPP IV) (CD26) plays a critical role in the modulation and expression of autoimmune and inflammatory diseases. We recently reported that sera from patients with rheumatoid arthritis and systemic lupus erythematosus contained low levels of DPP IV and high titers of anti-DPP IV autoantibodies of

the immunoglobulin A (IgA) and IgG classes and found a correlation between the low circulating levels of DPP IV and the high titers of anti-DPP IV autoantibodies of the IgA class. Since streptokinase (SK) is a potent immunogen and binds to DPP IV, we speculated that patients with autoimmune diseases showed higher DPP IV autoantibody levels than healthy controls as a consequence of an abnormal immune stimulation triggered by SK released during streptococcal infections. We assessed this hypothesis in a group of patients suffering from acute myocardial infarction, without a chronic autoimmune disease, who received SK as part of therapeutic thrombolysis. Concomitant with the appearance of anti-SK antibodies, these patients developed anti-DPP IV autoantibodies. These autoantibodies bind to DPP IV in the region which is also recognized by SK, suggesting that an SK-induced immune response is responsible for the appearance of DPP IV autoantibodies. Furthermore, we determined a correlation between high titers of DPP IV autoantibodies and an augmented clearance of the enzyme from the circulation. Serum levels of the inflammatory cytokines tumor necrosis factor alpha (TNF-alpha) and interleukin 6 (IL-6) increased significantly after 30 days of SK administration, while the levels of soluble IL-2 receptor remained unchanged during the same period, suggesting a correlation between the lower levels of circulating DPP IV and higher levels of TNF-alpha and IL-6 in serum in these patients.

*Journal of Clinical Rheumatology 2002; 8: S-52*

## Behcet's disease and chronic oral ulcers patient present high levels of deglycosylated anti-lipoteichoic ACID-IGG.

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**Objetivo:** To assess the tumoral immune response against Lipoteichoic acid (LTA) and lipopolysaccharide (LPS), in two groups of patients with Behcet's disease (BD) (ChBD=Chilean BD patients, and BBD= Brazilian BD patients), and compared it to a group of patients with chronic benign oral ulcers (OU), and to normal controls.

**Methods:** Total serum IgG and IgA, anti-LTA IgG and IgA, and anti-LPS IgG and were assayed by ELISA. A radioimmunoassay to evaluate the capacity of immune complexes anti-LTA IgG and LTA to activate complement C5 to C5a was also used. Purified human serum lectin mannan binding protein (MBP) was used to quantify the degree of exposed mannose residues in the Fc region of anti-LTA IgG in the four groups.

**Results:** The median of the MBP binding capacity of the anti-LTA IgG antibodies was 0.417 ug MBP/ug IgG in ChBD, 0.526 ug MBP/ug IgG in BBD, 0.65 ug MBP/ ug IgG in OU, and 0.12 ug MBP/ ug IgG in normal controls. The difference between each BD group versus normal control was statistically significant, as well as the differences between OU group and controls ( $p < 0.0001$ ). No differences in

complement activating capacity were found between patients in those groups. The median of the serum levels of the anti-LPS IgA and IgG antibodies were significantly higher in the OU group than in normal controls ( $p < 0.023$ ), however no differences were found between each BD group and normal controls.

Conclusions: BD and OU presented significantly higher titles of deglycosilated anti-LTA IgG than normal controls, but only the OU group of patients presented significantly higher anti-LPS antibodies than normal controls. Our data suggest that LTA may be an important antigen in self-perpetuation of local damage in-patients with OU and BD.

*Annals of Rheumatic Diseases 2002; 61: 379-80*

## Influence of 308 TNF promoter polymorphism on the responsiveness of infliximab in patients with rheumatoid arthritis.

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Objective: The aim of this study is to investigate the association of the -308 tumor necrosis factor (TNF) promoter polymorphism (TNF1 -G/G-; TNF2 -G/A or -A/A-) with the clinical response to the administration of the chimeric monoclonal antibody against TNF (infliximab) in patients with rheumatoid arthritis (RA).  
Methods: We recruited 20 RA patients (10 G/A=Group 1, and 10 G/G= Group 2, for the -308 TNF- $\alpha$  genotypes) from the same geographic area. Genotyping for TNF promoter was performed by a method based

on PCR-RFLP analysis using amplification-created restriction site. All patients received 3 mg per kilogram of infliximab at the initiation of treatment (week 0) and weeks 2, 6 and 14, and were evaluated at day 0 and before each dose. Evaluators were unaware of the genetic background of each patient.

Results: The ACR 20 response was achieved by 100/90% of patients from group 1/group (G1/G2) at week 2 (no significant = n.s.), 100/70% G1/G2 at week 6 ( $p < 0.06^*$ ), and 100/89% G1/G2 at week 14 (n.s.). The response was achieved by 40/40% G1/G2 at week 2 (n.s.), and 100/78% G1/G2 at week 14 (n.s.). Between G1/G2, the decrease in the number of swollen and tender joints, was n.s. in both groups, a significant difference was observed for the patient's assessment of pain, 63/47% G1/G2 at week 6 ( $p < 0.09^*$ ), and 83/34% G1/G2 at week 14 ( $p < 0.02^*$ ) respectively.

Conclusion: Both groups showed a significant improvement with treatment. When patients from group 1 and 2 were compared, no differences were found for most of the parameters studied, however patients from group 1 showed a significant improvement in some of the variables studied.

# Antinucleosome Autoantibodies in Rheumatoid Arthritis (RA) Patients Treated with Methotrexate (MTX) or TNF Antagonists: Prevalence, Clinical and Serological Correlations

Category: 16 RA-clinical aspects Raquel S Cuchacovich<sup>1</sup>, Diana Flores<sup>2</sup>, Abraham Gedalia<sup>2</sup>, Miguel Cuchacovich<sup>3</sup>, Javier Marquez<sup>2</sup>, Ranju Singh<sup>2</sup>, Hilary Thompson<sup>2</sup>, Yamini Menon<sup>2</sup>, Maureen Vincent<sup>2</sup>, Eve Scopelitis<sup>2</sup>, Mario Garza<sup>4</sup>, Luis R Espinoza<sup>2</sup>  
<sup>1</sup>LSU Health Sciences Center, Rheumatology Section, New Orleans, LA; <sup>2</sup>LSU Health Sciences Center, New Orleans, LA; <sup>3</sup>University of Chile, Santiago, Chile <sup>4</sup>Universidad Autonoma de Nuevo Leon, Monterrey, Mexico Presentation Number: 869 Poster Board Number: 334 Keywords: Rheumatoid Arthritis, Nucleosomes, TNF antagonists

Evidence accumulated suggests that the nucleosome, the fundamental unit of chromatin and normal product of cell apoptosis, plays a key role in human lupus, however, little is known about antinucleosome antibodies and RA, especially following the use of biological agents.

Objective: To study the frequency, clinical and serological correlations of antinucleosome antibody reactivity in RA patients treated with TNF antagonists or MTX followed up for 5 years.

Patients and Methods: A total of 88 RA patients mean age 48.7 (SD 16.5) and mean disease duration 8.23 (SD 8.1) years, all fulfilling ACR criteria for RA and 70 healthy controls matched in age and sex were studied.

Clinical records and laboratory data of the patients have been maintained at LSUHSC since 1997, 26 patients were treated with TNF and 62 with MTX. A semi-quantitative ELISA assay for nucleosome reactive antibodies was performed in triplicate; ANA, ENA panel, ds DNA, RF, ANCA, CRP, and ESR were concomitantly done. Clinical and serological evaluations were performed before and after the use of MTX or biological agents. Also number of swollen joints, physician (PGA) and patient global (GAP) assessment, functional class and disease activity were evaluated. Analysis was based on logistic regression.

Results: Of the total group 36/88 (40.9 %) were seropositive for antinucleosome antibodies, as compared to none in the healthy controls, 12/26 (46%) in the TNF group, and 24/62 (38.7%) under MTX were antinucleosome antibodies positive. Statistically significant correlations were found in both groups with ANA (OR: 4.8 p: 0.0003), PGA (p: <0.001), GAP (p: <0.001), number of swollen joints (p: <0.001), and functional activity (p: <0.05). When the variable time was included de novo dsDNA (p: 0.0283) positivity was significant; also statistically significant was treatment over time (MTX vs TNF) and disease activity (p: 0.0063) meaning that patients treated with MTX have 3.5 likelihood to be active at 5 years on comparison with the ones treated with TNF antagonists. Analysis of disease activity in antinucleosome positive treated with TNF or MTX showed that antinucleosomal seropositivity was associated with anti-TNF induced remission (p: 0.0348). In this population antinucleosomal antibodies emerged prior to dsDNA antibodies.

Conclusion: Approximately half of the RA patients exhibit antinucleosome antibodies, and its presence inversely correlates with disease activity. TNF antagonists therapy induced apoptosis may explain in part the develop-

ment of antinucleosomes and dsDNA antibodies in these patients; and also antinucleosomes may represent an early marker of responsiveness to TNF antagonist therapy.

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## Analysis of antinucleosome antibodies in systemic lupus erythematosus (SLE) patient of different ethnicity: prevalence, clinical and serological correlations.

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There is now strong evidence that the nucleosome is both the driving immunogen and the in vivo target of lupus anti-ds DNA and antihistone antibodies. The presence of nucleosome-specific antibodies has been demonstrated in human lupus and appears to be the major target antigens. Some studies suggest a positive correlation between renal involvement and these autoantibodies.

Objective: To study the prevalence of their clinical and serological impact in three different ethnic groups.

Patients and methods: Serum samples from 99 SLE patients mean age 41 and mean disease duration 6.5 years, (53 African American (AA), 27 Hispanic (H), 19 Caucasian (C) ), all fulfilling revised ACR 1997 criteria and 12 healthy controls matched in age and sex were prospectively studied. A semi-quantitative ELISA detection of chromatin reactive anti-

bodies was performed in triplicate (QUANTA Lite Chromatin, ANOVA). Clinical activity of SLE was determined by SLEDAL, and ECLAM in half of the patients, ANA, ENA, ds DNA, Complement levels, anti-cardiopin, CRP, and routine lab were obtained at the same time of the clinical evaluation.

Results: Of 99 SLE patients 65.7% were seropositive for antinucleosome antibodies, as compared to none of the controls. Frequency was similar in the all ethnic groups. No correlation with ethnicity, age, disease duration was found. When comparing the nucleosomal (+) 64/99 with the negative group 35/99, a statistical significant correlation was found for ANA, ds DNA, complement levels disease activity indices and CNS involvement ( $p < 0.001$ ). No correlation was found with other antibodies, clinical features and treatment. Among different ethnic groups AA showed a positive correlation with ANA, ds DNA, complement levels and hematological involvement ( $p < 0.001$ ). In the Hispanic group complement levels were significantly related ( $p < 0.001$ ), while in the Caucasian group ds DNA was significantly correlated ( $p < 0.001$ ).

Conclusion: Antinucleosome antibodies were present in 2/3 of SLE patients, and were strongly associated to ANA, ds DNA, hypocomplementemia (C3-C4) and CNS and hematological involvement.

## Lack of detection and expression of human retrovirus 5 in patients with psoriatic arthritis (Ps A) and rheumatoid Arthritis (RA)

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Accumulated evidence suggest that retroviruses may play a role in the pathogenesis of certain autoimmune disorders. In addition, particles resembling retroviruses have been reported in tissue and synovial fluid from patients with psoriasis and rheumatoid arthritis. Human Retrovirus (HRV) is a oncovirus, probably endogenous with no endogenous retroviruses (ERV) homologues in the human DNA, HRV-5 pol sequence has been detected in one SS, one SLE and in three patients with brain tumor; but the results of the studies using PVR assay for proviral DNA are diverse.

Objective: To study the presence and expression of human retrovirus 5 in two autoimmune disease, Psoriatic Arthritis (Ps A) and Rheumatoid Arthritis (RA).

Material and Methods: Peripheral blood samples (PBMC) were obtained from 31 PsA, 21 RA patients and healthy controls matched in age and gender, PsA patients (mean age 43.8 + SD 15 years; mean disease duration 6.2 + SD 5.4 years) all fulfilled Moll and Wright's criteria, 27/31 had active joint and skin involvement, and the treatments were Methotrexate 11/31, NSAIDs 15/31, anti-TNF receptor 2/31 and 3/31 no treatment. RA patients (mean age 50.9 + SD 13.2 years; mean disease duration 12.4 +

SD 9.6 years) met ACR criteria, 12/21 were active and the treatment included Methotrexate, Prednisone and NSAIDs HRV-5 DNA and mRNA were tested by nested RT-PCR with adequate primers for HRV-5 pol region. To examine the contamination of proviral DNA, samples containing mRNA without RT were also amplified under the same conditions.

Results: HRV-5 proviral DNA in samples from all the patients and controls was negative. Expression of HRV-5 mRNA was also undetectable in the patients and controls.

Conclusions: There is no association between HRV-5/PsA and HRV-5/RA in the studied population. Our findings further corroborate previously published data, and provide support for existing evidence demonstrating a lack of role for HRV-5 in PsA and RA.

## Presence and expression of human endogenous retroviruses (HERV) in patients with Psoriatic arthritis (PSA)

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Objective: To determine the presence of HERV clones 3-1 and 4-1 DNA and the expression of mRNA HERV clones 3-1 and 4-1, in peripheral blood mononuclear cells (PBMC) from psoriatic patients, and also to compare them with healthy controls.

Patients and Methods: 34 Patients with PsA (mean age 51.1 ± SD 14.9 yr, disease dura-

tion skin 14.3 and articular 7.1 yr) were recruited from our Rheumatology clinics; all fulfilled Moll and Wright's criteria for PsA. PBMC were collected from 34 patients with PsA, and frozen at -70 C until tested. The clinical features were: polyarticular 18, oligoarticular 16, axial 9, skin 21 and nails 9. Treatment: Methotrexate 89, Sulphasalazine 2, NSAID 7, no treatment 1. Nine control samples were obtained from age and sex matched healthy volunteers. Samples were analyzed for the presence of DNA and RNA with the use of a one step RT-PCR with adequate primers of clones 4-1 gag region and 3-1 pol region. To examine the contamination of proviral DNA, samples containing mRNA without RT were also amplified under the same conditions.

Results: DNA of clones 3-1 and 4-1 was detected in all PsA and controls. In contrast, mRNA expression of clones 3-1 and 4-1 was undetectable in all of the PsA patients regardless of disease activity and treatment received. In the control group mRNA clone 3-1 was expressed in all of them, and mRNA clone 4-1 was expressed in 4/9.

Conclusion: Lack of mRNA expression of HERV clones 3-1 and 4-1 in PsA patients may be the result of the underlying immune dysregulation seen in these patients, and may adversely influence the outcome of infections with the same HERV or exogenous retroviruses, or other microorganisms.

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## TH1/TH2 cytokine mRNA expression in rheumatoid arthritis (RA) and psoriatic arthritis (PSA) patients

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The role of T cells in psoriatic and rheumatoid arthropathies are not fully understood, but the observation that arthritis improves in patients with PsA and RA who receive T cell inhibitors and the association of class II MHC alleles with both diseases, suggest that lymphocytes participate in their pathogenic processes.

Objective: To determine patterns of cytokine mRNA expression in peripheral blood mononuclear cells (PBMC), synovial tissue (ST) and skin (5) from patients with PsA and RA; as well as to determine their differential expression according to disease activity and to compare their profile of cytokine expression with normal controls.

Material and Methods: Patients with PsA and RA were recruited from our Rheumatology clinics; all fulfilled Moll and Wright's criteria for PsA and ACR criteria for RA. ST, S and PBMC were obtained the same day, and frozen at -70 C until tested. Spontaneous cytokine mRNA expression of interferon-gamma (IFN- $\gamma$ ), Tumor necrosis factor-beta (TNF- $\alpha$ ) and IL-4 of ST, S, and PBMC were determined using a semi quantitative RT-PCR, also healthy controls were studied. Quantification of cytokines by RT-PCR was carried out comparing the intensity of each band to Glycerolaldehyde-3-phosphate-dehydrogenase mRNA expression.

Results: Twenty patients with PsA mean age 38  $\pm$  SD 11.7 years, thirteen with RA mean age

## Urología

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*American Urologic Association 71st annual meeting;  
204 (P-C2)*

### Initial Results of a New Advancement in high temperature Cooled Thermotherapy (TUMT) treatment for Benign Prostatic Hyperplasia (BPH)

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Introduction: Subjects were enrolled in a clinical study of a new generation of high temperature cooled thermotherapy (TUMT) treatment catheter (Cooled ThermoCath™) with an advanced cooling system. The new cooling system allows for a high temperature treatment that increases the zone of necrosis and treatment efficacy without compromising the safety and comfort of the patient.

Methods: Thirty-four men, 45-85 years of age, AUA score > 8, peak flow rate < 15 ml/sec, underwent a single 28.5 minute high-temperature treatment using the Cooled ThermoCath. Treatments were performed on an outpatient basis with minimal oral and topical analgesics. Subject tolerance was measured by using a Visual Analog Scale (VAS). One week post-treatment the volume of necrosis was measured by MRI. Follow-up evaluations were completed at 1 week, 6 weeks, 3 months and 6 months using AUA and QOL scores and Qmax.

52 ± SD 7.5-years and 15 controls mean age 34.1 ± SD 12.3 were studied. IFN-γ mRNA and TNF-β mRNA and IL-4 mRNA expression were significantly higher in RA vs PsA patients ( $p < 0.001$ ). IL-4 mRNA was not identified in the control group and was expressed in only 2/20 PsA. Active psoriatic skin and/or joint involvement was present in 16 (80%) patients, and absent in 4 (20%); active RA was present in 8/13 (61%) and absent in 5/13 (39%). Disease duration did not differ significantly between both groups. IFN-α mRNA were detected in 10/16 active (63%), and in 3/4 inactive (75%) PsA; and the levels of expression were not significantly different between the two groups ( $p = > 0.5$ ). The expression, however, of IL-4 mRNA was not detected in the active PsA group, but 11/4 patients with inactive PsA expressed high levels of IL-4. The expression levels of IFN-γ, TNF-β and IL-4 mRNA did not differ significantly among RA patients, but the IFN-γ, TNF-β and IL-4 mRNA expression were significantly higher in RA vs controls ( $p < 0.001$ ) and not significant in PsA vs controls.

Conclusion. Dysregulation of the TH1/TH2, cytokine profile is present in RA, and a prevalence of a TH1 pattern is seen in PsA; therefore these cytokines could be another molecular target for novel therapeutic strategies.



Results: The mean prostatic size was 46.3 grams. The necrosis volume one-week post treatment was 8.8 (mm<sup>3</sup> x 1,000), compared to 7.3 as reported in a previous Targis@ 60-minute trial. The maximum VAS score during the treatment was 3.3, with a mean of 1.0. At six months, AUA score decrease 78% from a baseline of 21.2 to 4.7 while QOL improved 87% from 4.7 to 0.6. Peak flow increased from 10.2 to 12.4 ml/sec. Minimal adverse events were reported.

Conclusion: The Cooled ThermoCath provided superior results to the existing Targis catheter technology. Long-term follow-up is necessary to evaluate durability of results.

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## Histologic analysis of prostate tissue after ablation using permanently implanted thermal rods.

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Introduction and Objectives: We have evaluated the histological tissue destruction of the human prostate induced by thermal rod therapy for prostate cancer. The technique involves the transrectal ultrasound guided placement of permanent temperature self-regulating rods in the prostate; the rods are then heated an extra corporeal alternating magnetic field. Various rod temperatures, treatment times and implantation schemes were evaluated in relation to the histological tissue destruction.

Methods: Twenty-four patients with biopsy confirmed cancer that were scheduled for radical

prostatectomy were first given thermal therapy. The standard was performed 4 to 60 days after the thermal treatment. Histological analysis performed on whole mount specimens. Sections were taken with the rods in order to correlate the rod location to the histological changes. Variables investigated were: rod operating temperatures of 55, 60 and 70°C; various treatment times (15 to 60 min); multiple treatments (1, 2 or 4); and various implantation densities and rod locations.

Results: Twenty-four patients were treated and analyzed. Single rods produced necrosis (55 and 60°C) or variably shaped necrosis (70°C). Arrays of 55 and 60°C rods produced non-confluent necrosis around each rod. Arrays of 70°C rods placed end-to-end, within 1 cm of each other produced consistent necrosis inside array. At the edge of the array temperatures dropped off quickly and necrosis limited to 1 to 2 mm from the rods placed at the capsule. Urethra endothelium preserved if rods were placed 5 to 10 mm from the urethra. Necrosis varied from complete coagulation necrosis with the loss of normal architecture to organized cells with damaged nuclei. A single treatment of 1 hour was necessary to produce consistent necrosis.

Conclusions: Treatment with arrays of 70°C rods for 60 min produces consistent destruction of large volumes of prostate tissue even up to the capsule without damaging surrounding tissue.

## Interstitial thermal therapy in patients with localized prostate cancer: histologic analysis.

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**Objectives:** To examine, by way of histologic examination, the destruction of excised prostate glands treated with thermal ablation. Thermal ablation treatment with permanently implanted temperature self-regulating rods is being used in the treatment of localized prostate cancer. **METHODS:** Four patients with biopsy-proven prostate cancer, who had been scheduled for routine radical prostatectomy with a gland size of less than 70 g, Gleason sum of 7 or less, and prostate-specific antigen values less than 10.0 ng/mL, were implanted with 70 degrees C rods under ultrasound and fluoroscopic control. The patients were then given multiple thermal treatments. Glands were removed and histologically analyzed to assess the thermal destruction. **Results:** Histologic examination revealed confluent thermal destruction within the rod array when the rods were placed end-to-end and no farther than 1 cm apart. Little necrosis was seen outside the array. To ensure the necessary destruction, the rods must be placed at the capsule, including posteriorly near the rectum. The results indicated that energy levels greater than 40 W-min/g of tissue should be used. This can be achieved by implanting 1.5 rods/g of prostate and treating the patient for 60 minutes. In 3 of the 4 patients, no residual cancer was found in the gland after thermal treatment. **Conclusions:** Histologic examination has aided in determi-

ning the implant density and treatment time and, therefore, the necessary energy, for adequate necrosis. The technique demonstrates the ability to destroy the prostate adequately, including tissue at the capsule. This new procedure appears promising in the treatment of localized prostate cancer.

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## Cyst of the prostatic utricle: report of a case complicated by giant lithiasis.

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**Objective:** We report a case of prostatic utricle cyst complicated with giant lithiasis. **METHOD/RESULTS:** A 42 year old man with history of surgery for bilateral cryptorchidism and hypospadias in his infancy, presented with initial and terminal hematuria and a digital rectal examination showing a rocky, smooth enlargement of the anterior rectal wall. Prostatic specific antigen was normal. Transrectal and transabdominal ultrasound showed a large retrovesical calcification and intravenous pyelogram showed normality of the upper urinary tract. The patient underwent a complete resection through a suprapubic extraperitoneal approach without complications. Histopathology revealed a 10 cm long prostatic utricle cyst complicated with lithiasis. **CONCLUSIONS:** The prostatic utricle cysts are rare in clinical practice and associate with anomalies of testicular descent and hypospadias. They have a difficult differential diagnosis and indication for treatment depends on presenting symptoms, size and complications.