Trabajos enviados a Congresos y/o publicados en revistas Internacionales por los profesionales del Hospital Clínico Universidad de Chile durante el año 2003.

Banco de Sangre

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Evaluación del proceso de selección de donantes de sangre

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Introducción: El proceso de selección del donante de sangre es un aspecto fundamental en la seguridad transfusional. Este proceso permite identificar antecedentes clínicos y conductas del donante que lo expongan a un riesgo al donar o se constituyan en riesgo para el receptor de adquirir alguna infección. Entonces, el cumplimiento o no de los criterios de selección permite aceptar o rechazar al eventual donante de sangre.

Objetivos: 1) Conocer el porcentaje de rechazo de donantes y sus causas.2) Comparar este resultado con el estándar establecido. (menor a 15%) 3) Desarrollar estrategias de intervención tendientes a mejorar los aspectos deficitarios detectados.

Método: El proceso de selección se lleva a cabo mediante una entrevista personal y privada realizada por un Tecnólogo Médico del Banco de Sangre capacitado para estos fines. En el caso de donantes rechazados, el registro incluye los siguientes elementos: Causa, categoría de causa (definitiva o transitoria),y profesional.

Se construyo un indicador de calidad que pretende dar cuenta del porcentaje de rechazo existente en el BSUCH, cuya formula es:

$$\frac{\text{N° de donantes rechazados}}{\text{N° total de donantes atendidos}} \times 100$$

Resultados y Conclusiones: El año 2002 el resultado fue de 14,2%, encontrándose dentro del estándar, pero sobre años previos. Las causales mas frecuentes de rechazo fueron hipertensión arterial, anemia y antecedente de tatuaje. Un porcentaje alto de rechazo se debió a la labor de una profesional recién incorporada, por lo cual se realizó la intervención para capacitarla adecuadamente.

Nuestros resultados son similares a los de otros países, pero diferentes a los que muestran centros que cuentan con donantes voluntarios altruistas.

Vigilancia activa de reacciones adversas inmediatas a la transfusión sanguínea.

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Introducción: La transfusión se asocia a riesgos inherentes al uso de componentes sanguíneos alogénicos.

El Banco de Sangre del Hospital Clínico de la Universidad de Chile (BSUCH) debe cumplir de manera rigurosa todas las etapas de manejo de la sangre. El cumplimiento de estos procesos permite evitar y reducir al mínimo las reacciones adversas a la transfusión inmediatas (RAT). Objetivos: 1)Conocer la frecuencia y causas de RAT durante el periodo Enero-Diciembre 2002, y luego comparar el resultado con el estándar establecido (menor a 1%) 2) Definir estrategias factibles de intervención para prevenir su ocurrencia. Método: Para su realización implementamos a partir del año 2000 un sistema de recolección de datos desde la ficha clínica, realizado por un Tecnólogo Médico quien diariamente emite un informe de aquellos pacientes en

que se detecta algún tipo de RAT. Este informe es entregado al Médico del BSUCH para su verificación y diagnóstico final.
El indicador evaluado es el índice de reacciones adversas a la transfusión relacionando:

$$\frac{\text{N° de Reacciones Adversas a Transfusión x 100}}{\text{N° de hemocomponentes transfundidos.}} =$$

Resultados y Conclusiones: Al implementar la vigilancia activa de las RAT, se constató que existía un subregistro. Durante el período estudiado el porcentaje de RAT fue de 0.48%. (59 RAT en 12.321 componentes transfundidos). Correspondieron 38 a reacciones transfusionales febriles no hemolíticas (RTFNH), 11 a reacciones alérgicas, 10 a calofríos. Todas ellas se manejaron con terapia adecuada. Estos resultados están dentro del estándar esperado.
9 de 59 reacciones se presentaron en pacientes que habían recibido componentes desleucocitados, 3 de 9 fueron RTFNH asociadas a transfusión de plaquetas filtradas.

Cirugía

Dis Esophagus. 2003; 16(1): 24-8.

Prevalence of intestinal metaplasia according to the length of the specialized columnar epithelium lining the distal esophagus in patients with gastroesophageal reflux.

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The diagnosis of Barrett's esophagus is based on the presence of intestinal metaplasia (IM) at the distal esophagus. The aim of this study was to determine the prevalence of IM in patients with symptoms of gastroesophageal reflux in whom endoscopically a segment of distal esophagus was covered by columnar epithelium (CE). In a prospective, descriptive and transversal study, 492 patients (33%) from 1480 patients with gastroesophageal reflux, in whom endoscopic evaluation demonstrated the presence of a short-segment CE measuring less than 3 cm or a long-segment CE measuring more than 3 cm, were evaluated. From each patient, several biopsy specimens were taken, which were stained with hematoxylin-eosin and Alcian blue pH 2.5. Out of 492 cases, 421 patients (86%) presented with a short-segment CE and 71 patients (14%) had a long-segment CE. Among these 71 cases, 38 had a 3-6 cm-length CE, 21 patients had a 6.1-10 cm-length CE and 12 patients had CE more than 10.1 cm in length. Endoscopic short-segment CE was six times more frequent than long-segment CE. The prevalence of IM was 35% among patients with short-segment CE and increased progressively according to the length of CE, being 100% in patients with > 10 cm in length. Therefore, true short-segment BE was three times more frequent during endoscopic studies than long-segment BE. Dysplasia in the metaplastic epithelium also increased parallel to the length of the CE. True BE (presence of IM at the columnar epithelium lining the distal esophagus), was present in 13.6% of all patients with symptoms of gastroesophageal reflux submitted to endoscopic evaluation. Short-segment BE is three times more frequent than long-segment BE, and endoscopic and bioptic evaluation is fundamental in all cases with gastroesophageal reflux who exhibit some segment of the distal esophagus lined by columnar epithelium, even if it is > or = 1 cm long.

J Gastrointest Surg 2003; 7: 237-44; discussion 244-5.

Transcriptional activation of the enterocyte differentiation marker intestinal alkaline phosphatase is associated with changes in the acetylation state of histone H3 at a specific site within its promoter region in vitro.

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Enterocyte differentiation is thought to occur through the transcriptional regulation of a small subset of specific genes. A recent growing body of evidence indicates that post-translational modifications of chromatin proteins (histones) play an important role in the control of gene transcription. Previous work has demonstrated that one such modification, histone acetylation, occurs in an in vitro model of enterocyte differentiation, butyrate-treated HT-29 cells. In the present work, we sought to determine if the epigenetic signal of histone acetylation occurs in an identifiable pattern in association with the transcriptional activation of the enterocyte differentiation marker gene intestinal alkaline phosphatase (IAP). HT-29 cells were maintained under standard culture conditions and differentiated with sodium butyrate. The chromatin immunoprecipitation (ChIP) assay was used to compare the acetylation state of histones associated with specific regions of the IAP promoter in the two cell populations (undifferentiated vs. differentiated). Chromatin was extracted from cells and cleaved by sonication or enzymatic digestion to obtain fragments of approximately 200 to 600 base-pairs, as confirmed by polymerase chain reaction using primers designed to amplify the IAP segments of interest. The ChIP assay selects DNA sequences that are associated with acetylated histones by immunoprecipitation. Unbound segments represent DNA sequences whose histones are not acetylated. After immunoprecipitation, sequences were detected by radiolabeled polymerase chain reaction, and the relative intensity of the bands was quantified by densitometry. The relative acetylation state of histones at specific sites was determined by comparing the ratios of bound/unbound segments. We determined that in a segment of the IAP promoter between -378 and -303 base-pairs upstream from the transcriptional start site, the acetylation state of histone H3 increased twofold in the differentiated, IAP expressing cells, whereas that of histone H4 remained essentially constant. Additionally, at a distant site, between -1378 and -1303 base-pairs, the acetylation state of H3 and H4 did not change appreciably between the undifferentiated and differentiated cells. We conclude that butyrate-induced differentiation is associated with specific and localized changes in the histone acetylation state within the IAP promoter. These changes within the endogenous IAP gene may underlie its transcriptional activation in the context of the enterocyte differentiation program.

J Gastrointest Surg 2003; 7:1053-61; discussion 1061.

Convergence of the thyroid hormone and gut-enriched Kruppel-like factor pathways in the context of enterocyte differentiation.

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The gut-enriched Kruppel-like factor (KLF4) and the ligand-bound thyroid hormone receptor (TR) have each been shown to play a critical role in mammalian gut development and differentiation. We investigated an interrelationship between these two presumably independent pathways using the differentiation marker gene, intestinal alkaline phosphatase (IAP). Transient transfections were performed in Cos-7 cells using luciferase reporter plasmids containing a 2.5 kb segment of the proximal human IAP 5' regulatory region, as well as multiple deletions. Cells were cotransfected with TR and/or KLF4 expression vectors and treated+/-100 nmol/L thyroid hormone (T3). IAP reporter gene transactivation was increased independently by KLF4 (ninefold) and ligand-bound TR beta 1 (sevenfold). Cells cotransfected with KLF4 and TR beta 1 in the presence of T3 showed synergistic activation (70-fold). A similar pattern was seen with the other T3 receptor isoform, TR alpha 1. The synergistic effect was lost with deletions of the T3 and KLF4 response elements in the IAP promoter and was completely or partially abolished in the case of mutant

KLF4 expression vectors. The thyroid hormone receptor complex and KLF4 synergistically activate the enterocyte differentiation marker gene IAP, suggesting a previously unrecognized interrelationship between these two transcription factor pathways.

Surgery 2003; 133: 364-7.

Length of the esophagus in patients with gastroesophageal reflux disease and Barrett's esophagus compared to controls.

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Background: It is a current opinion among surgeons that the esophagus is shorter in patients with reflux disease and particularly in those with complicated Barrett's esophagus. However, objective evidence of this is scarce. Therefore we attempted to determine the occurrence and magnitude of this phenomenon among our patients. Methods: One hundred ninety control subjects, 77 patients with severe erosive esophagitis, 74 with Barrett's esophagus, and 29 with complicated Barrett's esophagus (ulcer, stenosis) were grouped according to height. The length of the esophagus was determined by standard manometric study, measuring the distance from the crycopharingeal sphincter to the distal limit of the lower esophageal sphincter. Values were expressed in cm as the mean +/- SD. RESULTS: The esophageal length according to height was 1 to 2 cm shorter in patients compared to controls, but these differences were not significant. Conclusions: No differences were found between patients with progressive severity of the disease. This study confirms that the presence of a so-called "short esophagus" does not exist or is not relevant in our patients with gastroesophageal reflux disease, including those with complicated Barrett's esophagus.

Wordl J Surg 27, 1235-1240, 2003

Pancreatic Autotransplantation in Chronic Pancreatitis

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The pancreatic state secondary to resective surgery for chronic pancreatitis is associated with a high rate of late morbidity and mortality that is due, in part, to endocrine insufficiency. Resective procedures should, therefore, be used very selectively. Over the last 2 decades we have seen a shift from extensive distal resections to limited proximal resections. This because of the lowering of the operative mortality of pancreatic head resection and its better results in pain relief, while preserving in situ the body and tail the gland with its metabolic functions. Islet Autotransplantation and segmental pancreatic Autotransplantation were introduced in 1977 and 1978, respectively. Over 150 and 25 cases operations have been reported, respectively. Both techniques are evolving with a goal to improve results. Procedures placing the graft in the aliac fossa and anastomosing the pancreatic duct to the jejunum are now favored over groin placement and duct occlusion. Islet autotransplant achieve a higher yield of islet cells and decrease the exocrine impurity of the preparation. Both methods can prevent or delay to onset of diabetes mellitus, and when diabetes mellitus does accur, it is frequently easier to manage. The long term function of the grafts appears to the dependent of the b-cells mass available in the diseased pancreas, the loss of cells related to the transplant procedure, and the characteristics of gradual loss of function from the type of transplant used. Although extensive pancreatic resections are occasionally required, the possibility of Autotransplantation should be considered in those patients.

Int Surg 2003; 88: 159-63.

Management of common bile duct stones: the state of the art in 2000.

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Biliary lithiasis is a widespread disease all over the world; one-third of the white population presents stones in the biliary ducts. In Chile, it is present in 47% of adult females. The most common complications of this pathology are acute cholecystitis, choledocholithiasis, acute pancreatitis, retained common bile duct (CBD) stones, and Gallbladder cancer; these constitute a serious health problem in Chile. The aim of this study was to update the information related to choledocholithiasis after 10 years of laparoscopic biliary surgery. To achieve this objective, we retrospectively analyzed the last 100 cases of choledocholithiasis admitted to the Universidad de Chile Clinical Hospital in 2000. Prevalence by sex and age was determined. Clinical diagnosis was demonstrated to be effective in 92.3% of the cases; laboratory tests and ultrasound were effective in 81% and 90% of the cases, respectively. Diagnosis of cholelithiasis and choledocholithiasis as one unique entity corresponded to 53% of the sample; 47% of the remaining choledocholithiasis cases corresponded to retained CBD stones in patients previously cholecystectomized. Time of appearance of symptoms of this residual pathology was reviewed. All methods or procedures employed to treat this pathology were studied, and it was found that endoscopic cholangiography (ERCP) was the most frequently used procedure. Also, results of other alternative procedures, such as open surgery or ERCP combined with laparoscopic cholecystectomy, were considered. Finally, this study was complemented with a thorough bibliographic review of more than 100 publications on the subject that were published in high-impact surgical reviews, emphasizing the course of treatment followed during the last 7 years.

J Gastrointest Surg 2003 May-Jun; 7(4): 547-51.

Histologic findings of Gallbladder mucosa in 87 patients with morbid obesity without gallstones compared to 87 control subjects.

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Obesity is an important risk factor for the development of gallstones. The purpose of this study was to determine histologic alterations in the Gallbladder mucosa and the prevalence of gallstone disease in patients with severe and morbid obesity compared to histologic findings in the Gallbladder mucosa of control subjects. Two groups were studied: 125 severely obese patients (38 with and 87 without gallstones) and 87 control subjects. Ultrasonography was performed in all of them before surgery. During surgery, cholecystectomy was performed in 87 obese patients with a "normal" Gallbladder and in all 87 control subjects. Specimens were immediately sent for histologic analysis. The prevalence of gallstones was twice as high among obese women compared to obese men ($P < 0.001$). Normal Gallbladder mucosa was found in 28.7% of obese women compared to 34.2% of control women ($P > 0.59$). Findings were similar among the men. The most frequent histologic abnormality in the gallbladder mucosa among obese women was cholesterolosis (37%), followed by chronic cholecystitis and cholesterolosis (18%), with frequencies of 23% and 12%, respectively, in control women ($P > 0.1$). Among men, a similar proportion of histologic abnormalities was seen in obese men and control subjects. In our population of obese patients compared to control subjects, a similarly high proportion of histologic abnormalities of the Gallbladder mucosa was found in the absence of stones. These findings could have been attributed to the fact that the Chilean population has a high incidence of gallstones.

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.

Dis Esophagus 2000; 13:104-7; discussion 108-9.

Cardiomyotomy in achalasia: which fibers do we cut?

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Until now, it has not been quite clear which muscular fibers are cut when a cardiomyotomy for achalasia is carried out. In the present report, in a human achalasic gastroesophageal specimen, the mucosa of the stenotic segment was stripped off, allowing the fibers of the inner muscular coat to be seen. In addition, three cardiomyotomies at different sites were simulated. In achalasic specimens, the stenotic area is formed by the semicircular ('clasp') and oblique ('sling') muscular fibers. Different myotomies section these two muscular bands in distinct proportions. The stenotic segment in achalasia coincides topographically with the anatomic lower esophageal sphincter area. The site of cardiomyotomy is not irrelevant because this sphincter is not an annular muscle and the two muscular components of the sphincter can be sectioned in different ways. This may be important in post-operative results with regard to the relief of dysphagia and the appearance of gastroesophageal reflux.

J Gastrointest Surg 2002; 6: 645-52.

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.

Dermatología

Campaña de prevención de cáncer cutáneo en Santiago de Chile. Diagnóstico de lesiones pigmentarias malignas en 895 individuos examinados.

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En Octubre de 2002, se realizó una campaña de prevención y educación del cáncer cutáneo, denominada "Exposol", donde fueron examinadas 895 personas, de las cuales 70% eran mujeres. Las edades fluctuaban en tres 6 meses y 92 años con un promedio de 45 años.

El 8.9% del total fueron lesiones premalignas y malignas, con un 7.2% en el grupo de mujeres y un 13% en el grupo de hombres ($p<0.05$). El promedio de edad en personas con lesiones benignas fue de 43 años, a diferencia de los individuos con lesiones tumorales que fue de 61 años ($p<0.05$).

Un 33.8% de los tumores correspondieron a carcinomas basocelulares, 6,3% a melanomasa malignos, 1,3% a enfermedad de Bowen, 48,8% a queratosis actínicas. Presencia de carcinoma espinocelular y queratosis actínicas en la en la misma persona se encontró se encontro un 2,5%. La asociación entre carcinoma basocelular y queratosis actínica fue de 6,3% y entre melanoma y queratosis actínica 1,3%.

En conclusión los hombres presentan mayor incidencia de lesiones malignas y premalignas en el grupo estudiado, siendo más frecuentes este tipo de lesiones en personas de mayor edad confirmando la observación internacional. Las lesiones más frecuentes fueron QA y CBC. Cabe destacar el gran valor educativo que tiene este tipo de actividades, además de ser un adecuado instrumento para el diagnóstico precoz de lesiones malignas y premalignas.

Intenational Investigative Dermatology, Abril 2003, Miami, Florida.

Body site distribution of cutaneous tumors in Chile. Analysis of 4800 tumours from five major hospitals in Santiago

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The last 10 years have shown an increase of skin cancer incidence rates in Santiago. The purpose of this study was to analyse the anatomical localization of 4800 skin tumours. For this purpose, 600.000 histophological reports (1992-2001) from 5 hospitals belonging to the chilean Health Service Program were reviewed. These hospitals covered approximately a population of 2 million people. A total of 568 Malignant Melanoma (MM), 1,021 Squamous Cell Carcinoma (SCC) and 3,212 Basal Cell Carcinoma (BCC) were studied. Chi square test was used for the statistical analysis. MM in female was mainly foundin legs (23%), cheeks (19.7%) and foot (13.5%); however, MM in male was also mainly observed in middle face- area (12.9%), genital area (11.2%) ears (10.2%). BCC in females and males was mainly observed in the middle face-area (34.4%), cheeks (27.4%), and eyelids (10.3%).

Female showed significantly higher number of MM on the foot. Regarding age, patients over 50 years old shower higher number of MM in the face than those younger than 50 years old ($p<0.05$). Facial MM and facial BCC ($p<0.05$) show increase in the studied decade; however, SCC in the face tend to decline ($p<0.05$). The number of BCC and SCC was significantly higher in the face than in rest of the body, the opposite is observed in MM. Regarding the breslow Index (BI) m the MMs located in the face, truk, and legs were mainly BI: I: however, MMs located in arms, feet and soles were mainly BI: III and IV. These results are interesting, show concordance and differences with those reported in the literature. Genetics, environmental conditions and lifestyle factors may explain these findings.

Campaña de prevención del cáncer de piel: Experiencia HCUCh, Santiago, Chile.

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Considerando el incremento de cáncer de piel a nivel mundial y tomando en cuenta estudios nacionales que muestran dicho incremento gradual en los últimos años en Chile, en nuestro Departamento surgió una inquietud de medir el conocimiento general de nuestra población en relación al tema. Para lo anterior se diseño y realizó un proyecto destinado a la promoción de actividades preventivas en cáncer de piel, realizándose sesiones de exámenes dermatológicos gratuitos por parte de personal calificado a la población consultante en el marco de esta campaña. Se realizó una difusión masiva a través de distintos medios de comunicación (prensa, radio y televisión), lo que posibilitó una gran concurrencia de público a este evento.

Se evaluaron 2378 personas, mujeres (77%), entre 40-60 años (39%), en su mayoría dueñas de casa (34%), que acudieron de diversos puntos de Santiago y de otras ciudades de Chile.

Se presenta esta experiencia en términos de planificación, difusión y ejecución de una actividad destinada a medir conocimientos generales de una población dada así como también entregar algunos elementos educativos sobre cáncer de piel, cuyo impacto mediremos en futuras campañas.

Paniculitis granulomatosa. Rol de Microbacterias

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En octubre de 2002 y febrero de 2003 se presentaron aproximadamente 60 casos, en su mayoría mujeres entre 30 y 50 años que acudieron al mismo centro cosmetológico por tratamiento de lipodistrofia. Se les administró una sustancia inyectable, al parecer thiomucase asociado a un extracto de alcachofa.

Se presentan 8 pacientes mujeres sanas, 37 años de edad promedio, que consultaron 2 a 3 meses después de aplicarse esta sustancia por aparición de múltiples nódulos subcutáneos de 1 cm de diámetro, dolorosos eritematosos algunos drenando secreción caseosa. La biopsia mostró dermatitis y paniculitis crónica de tipo cuerpo extraño. Los estudios bacterológicos fueron negativos, excepto dos casos de baciloscopía positiva y un caso en el cual la baciloscopía y cultivo muestran bacilo alcohol-ácido resistente, con PCR compatible con Mycobacterium abscessus. En este caso, no hay respuesta satisfactoria al tratamiento con claritromicina y ciproflaxino por 5 meses.

Los procedimientos cosméticos pueden presentar complicaciones como infección de la herida operatoria y reacciones de hipersensibilidad. En caso de infección, los gérmenes habitualmente identificados incluyen S. Aureus y ocasionalmente otros microorganismos como las microbacterias de crecimiento rápido. Dado que sólo en uno de nuestros casos se demostró la presencia de Microbacterias, planteamos la posibilidad de que se trate de una respuesta de hipersensibilidad celular a alguna de las sustancias inyectadas, siendo el rol patógeno de las microbacterias controversial.

Epidemiología de carcinoma basocelular entre los años 1992-1998 en Santiago de Chile.

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En resumen se ha estudiado las incidencias del Melanoma Maligno y Cáncer Espinocelular en cuatro hospotales públicos de la Región Metropolitana en el período 1992-1998. En este estudio, 3759 Basocelulares (CBC) provenientes de estos hospitales fueron analizados. Se revisaron aproximadamente 330.000 informes histopatológicos, donde se utilizaron variables como la edad y sexo de los pacientes, localización, tipo clínico e histopatológicos del tumor. Se analizó la correlación entre el tipo clínico e histopatológico del tumor con la edad, sexo del paciente y localización del tumor. La localización del tumor fue estudiada en la cara (zona fotoexpuesta) y en el cuerpo. El número de CBC agresivos y las tasas de incidencia de CBC fueron estudiados por año. Se usó el test de Chi cuadrado para el análisis estadístico. El 56% de los pacientes con CBC eran de sexo femenino, 63% de los pacientes eran mayores de 65 años.

El tipo clínico más frecuente fue pigmentado (38,6%), el histopatológico más común fue el sólido (31,8%). El 71% de los CBC se localizaban en la cara (75% en mujeres, 68% en varones), solamente 8% de los tumores se clasificaban como agresivos histológicamente.

Se describe el aumento de la incidencia de los CBC a partir de la muestra observada a lo largo del períodp estudiado. Al igual que en el caso del Melanoma Maligno y del Carcinoma Espinocelular se observa un aumento de la tasa de incidencia del CBC entre los años 1992 y 1998. Las tasas fluctúan entre los 9,75 por 100.000 en 1998.

Múltiples estudios han mostrado la importancia de una política de prevención. De este modo se podría lograr prevención y/o un diagnóstico más temprano tratando de este modo las lesiones iniciales sospechosas. La Sociedad Americana de Dermatología fomentó la implementación del autoexamen de la piel y lograr de este modo la detección temprana de lesiones.

Se hace necesario implementar procesos efectivos de capacitación – dirigidos a población de riesgo,

para facilitar el autoexamen de sus lesiones y obtener una consulta precoz, ello redundará a una mejor vida de los pacientes y para el estado en menores costos de salud en técnicas quirúrgicas y paliativas.
Otros puntos a solucionar y que se han detectado en esta investigación son:
- Mejorar los registros de los informes anatomopatológicos,
- Mejorar la descripción del tipo histológico encontrado en los CBC diagnosticados,
- Especificar si el porcentaje encontrado es mixto,
Ampliar este estudio a las poblaciones de riesgo, aplicado a la totalidad del país. Buscando posibles variaciones de acuerdo a niveles de latitud en relación con la incidencia de mayores exposiciones a radiación HUV.
Los grupos de riesgos de CBC encontrados son mujeres mayores de 65 años y con lesiones ubicadas en zonas de fotoexposición intermitente (piernas) y fotoexposición continua (cara).
Este estudio es el análisis epidemiológico más grande de este tipo de tumor realizado en población chilena, con una muestra significativa de gran valor epidemiológico desde el punto de vista clínico. Lo cual nos debe llamar a prestar más atención sobre los patrones de presencias de CBC en la población chilena, dado el aumento significativo detectado en la población.

Validación de la técnica de electrocirugía en rinofima

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Rinofima es una enfermedad inflamatoria de la cara, del curso crónico y progresivo, etiología desconocida, se manifiesta en la tercera y cuarta década, con mayor incidencia entre los 50 y 60 años, frecuente en la mujer. Se expresa como papulopústulas que asientan en un fondo eritematoso con telagiectasias en la región centro-facial, complicaciones oculares y fimas. Dentro de estas ultimas, y principalmente en el hombre, puede desarrollarse una hipertrofia desfigurante en la nariz con importante repercusión estética y sicológica. El Rinofima es producto del aumento progresivo del tejido conectivo, hiperplasia de glándulas sebáceas, ectasia venosa e inflamación crónica profunda, con 4 variantes histológica: glandular, fibrosa, angiofibromatosa y actínica. Se seleccionaron 10 pacientes con Rinofima, edades entre 45 y 65, sin antecedentes mórbidos agregados. Fueron tratados mediados dermabrasión, electrocirugía convencional bajo anestesia local tumescente, en 3 ciclos separados por un lapso de 3 semanas. A los 14 días de la intervención se produjo repitelación cutánea, la regeneración total de las heridas se consiguió entre las 6 y 12 semanas. Todos los pacientes mostraron resultados aceptables sin complicaciones ni secuelas. El bajo costo del procedimiento, asociado a mínimas complicaciones y a excelentes resultados cosméticos hace de esta técnica una adecuada alternativa el tratamiento del rinofima.

Análisis de 925 tumores cutáneos infantiles diagnosticados histológicamente en un hospital pediátrico, Santiago de Chile.

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En nuestra población, el 9% de la consulta dermatológica infantil corresponde a tumores cutáneos. Con el objetivo de conocer la distribución de los diferentes tipos de tumores cutáneos infantiles, se analizaron 8.865 biopsias realizadas en el Hospital Roberto del Río, entre los años 1997 y 2001. Se registraron 925 tumores cutáneos, de los cuales 99,8% fueron benignos y 0,2% malignos. Los tumores cutáneos más frecuentes: nevo melanocítico adquirido (33,7%), nevo melanocítico congénito (25,1%), pilomatrixoma (17,8%), quiste dermatoide (3,9%) y quiste epidérmico (3,4%). Los nevos pilomatrixoma y quiste epidérmico predominaron en escolares y adolescentes y el quiste dermoide en lactantes y preescolares. Sólo en la pilomatrixoma se observó diferencias por género, con predominio en mujeres. El nevo melanocítico adquirido predominó en dorso de adolescentes y en pie de preescolares y escolares. El nevo melanocítico congénito predominó en cara de preescolares y escolares y en dorso de adolescentes. En este estudio, la

mayor frecuencia de tumores cutáneos en la infancia correspondió a nevos melanocíticos.

Un aporte en la clasificación y descripción de estadios histopatológicos del pilomatrixoma infantil

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La gran mayoría de los tumores en la infancia son benignos, Uno de estos es el pilomatrixoma, que tiene su diferenciación de células de la matriz del folículo piloso. Este tumor se considera un nódulo de consistencia dura o pétrea, recubierto de piel normal. Puede afectar cualquier parte del cuerpo, pero con mayor frecuencia la región de cabeza y cuello y extremidades superiores. Kaddu S y colaboradores han descrito una clasificación histológica del pilomatrixoma en cuatro etapas: Lesión temprana, Lesión bien constituida, Lesión regresiva temprana y regresiva tardía. Basados en esta clasificación, nosotros catalogamos los casos y propusimos un estadío más, que llamamos estadío final, caracterizado por hialinización u ozificación total. Estudiamos 277 plazas histológicas de niños entre 0 y 15 años, pertenecientes al Servicio de Anatomía Patológica del Hospital de Niños Roberto del Río. Encontramos que la mayoría de los casos 76,55 pertenecieron al estadío tardío (abundante calcificación y algunas veces osificación y poco o nada de infiltrado inflamatorio). Este hecho se confirma a pesar del corto tiempo de evolución y temprana edad de los pacientes. No encontramos relación significactiva de estos estadíos con edad, sexo, tiempo de evolución, ni tamaño del pilamatrixoma. Nuestros hallazgos apoyan la rápida evolución del tumor a estadíos regresivos tardíos o terminales y caracterizan a este tumor pediátrico de presentación frecuente.

Procedings XV Congreso Iberoamericano de Dermatología, Buenos Aires, Octubre 2003.

Eficacia y seguimiento en el largo plazo de pacientes con psoriasis vulgar moderada a severa en tratamiento con infliximab (Remidecade®).

Schroeder Francisca, Roizen Vicky, Vladés Pilar, Honeyman Juan, Sanchéz Leonardo.

Introducción: La psoriasis se presenta en forma moderada a severa en el 25% de los pacientes, requiriendo terapias sistémicas, no siempre exitosas. Infliximab es un anticuerpo monoclonal humano-murino anti TNF-α.
Se piensa que este mediador tendría un rol en la patogénesis de la psoriasis. Nuestro objetivo es evaluar la efectividad de la Infliximab en pacientes psoriáticos chilenos, con psoriasis extensa resistente a terapias convencionales.
Material y Método: Se realizó un estudio prospectivo, abierto siguiendo 8 pacientes con historia de psoriasis en la plaza extensa o eritrodérmica tratados con Infliximab 5 mg/Kg /dosis endovenosos en la semana 0,2 y 6. Los pacientes fueron controlados cada 2 semanas) cuantificando el PASI (Psoriasis Area and Severity Index), tomando fotografías y buscando reacciones adversas.
Resultados: El 100% de los pacientes respondieron al tratamiento dentro de las 10 primeras semanas. En la semana 10 se observa una disminución del PASI promedio del 88,6% (de 30,8 a 3,5). Seis pacientes requirieron dosis de refuerzo en un tiempo promedio de 37,3 semanas. Los eventos adversos más frecuentes fueron prurito y cefalea.
Discusión: Infliximab constituye una buena alternativa terapéutica para pacientes con psoriasis extensa o eritrodérmica refractaria a tratamientos de primera y segunda línea.

Localización Anatómica de tumores cutáneos. Análisis de 4800 casos tumores de hospitales públicos de santiago.

Zemelman V[1], Ruiz-Tagle J[1], Roa J[2], Valenzuela C[3], Honeyman J[1].
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El aumento del cáncer cutáneo en Santiago de Chile en la última década, nos motivó a estudiar la localización anatómica de 4.800 tumores cutáneos. Se revisaron aproximadamente 600.000 informes histopatológicos de 5 hospitales públicos de Santiago (1992-2001). Se estudiaron 568 melanomas malignos (MM), 1.021 Carcinoma Espinocelulares (CEC) y 3.212 Carcinoma Basocelulares (CBB). Se usó el test de Chi cuadrado para el análisis estadístico. Las principales localizaciones de MM en varones fueron y pie (29,2%%, tronco (16,5%) y brazos (16,5%); en mujeres fueron piernas (23%) mejillas (17,9%) y pie (13,5%). Para CEC, en varones fueron: área mediofacial (19,2%), mejillas (16,7%) y zona genital (11,8%); en mujeres: área mediofacial (12,9%), zona genital (11,2%) y orejas (10,2%). CBC, en varones y en mujeres ubicados principalmente en zona mediofacial (34,1%), mejillas (27,4%) y párpados (10,3%). Mujeres presentaban más MM en los pies ($p<0,05$). Se observó un aumento de MM faciales y una disminución de CEC faciales, mientras los CBC faciales no presentaban variación durante la década. Los MM en cara, tronco y piernas presentaban principalmente ÎNDICE Breslow (IB) I y II, en cambio MM acrales presentaban IB III y IV. Los resultados de este trabajo permiten establecer localizaciones de preferencia de cada tumor en población chilena, ayudando a orientar futuras campañas de prevención de esta neoplasia en nuestro país.

Tasas de incidencia Anuales de cáncer cutáneo en hospitales públicos de Santiago, Chile, década 1992-2001.

Zemelman V[1], Roa J[2], Muñoz P[1], Garmendia ML[3], Honeyman J[1].
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El aumento del cáncer de piel a nivel mundial nos motivó a estudiar las tasas de incidencia de cáncer cutáneo en cinco hospitales públicos de Santiago, Chile. Para este objetivo, se analizaron 600.000 informes histopatológicos de la década 1992-2001, en los servicios de Anatomía Patológica de estos hospitales. Estos hospitales cubren una población aproximada de 2.500.000 habitantes. Esto representa la mitad de la población de santiago y un 17% de la población de Chile. Se registró un total de 6.068 nuevos casos de tumores primarios; 658 Melanomas Malignos (MM), 1.468 Carcinomas Espinocelulares (CEC) y 3.942 Carcinomas Basocelulares (CBC). Se investigó la población asignada para cada hospital en cada año y se calcularon las tasas por 100.000 habitantes. Las masas de MM fluctuaron entre una mínima de 1.6 (1992) y una máxima de 3.52 / 100.000 en el año 1995. Las tasas de CEC fluctuaron entre 3.39 (1992) y 6.97/ 100.000 (1995). Las tasas de CBC variaron entre una mínima de 9.42 (1994) y una máxima de 21.5/ 100.000 (2001). Se obtuvo un aumento de un 52,3% de las tasas de MM, 90,9% de CEC y 119% de CBC en el año 2001 comparado con el año 1992. Las tasas de incidencia de cáncer cutáneo obtenidas en este trabajo son más bajas que las informadas por la literatura anglosajona, sin embargo muestran una preocupante tendencia al aumento en la década estudiada.

Endocrinología

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Proinsulin serum concentrations in women with polycystic ovary syndrome: a marker of beta-cell dysfunction?

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Background: The aim of this study was to establish the effect of polycystic ovary syndrome (PCOS) adjusted for adiposity on proinsulin concentrations. METHODS: Ninety-one women with PCOS and 72 normal cycling (NC) women were recruited. A 2 h, 75 g oral glucose tolerance test was performed. Glucose and insulin were measured in each sample. Proinsulin and C-peptide were determined at 0 and 30 min and the fasting proinsulin/insulin ratio (PI/I) was calculated. Insulin sensitivity was estimated by insulin sensitivity index (ISI) composite, and beta-cell function was estimated by insulinogenic index. Results: Insulin, proinsulin and C-peptide concentrations were higher in women with PCOS than in NC women ($P<0.05$). PI/I and insulinogenic index were similar in both groups. Proinsulin concentrations increased with body mass index ($P<0.05$) only in women with PCOS; therefore, proinsulin concentrations were higher in obese PCOS patients compared with obese control women ($P<0.05$). Moreover, a positive association between proinsulin concentrations and waist diameter adjusted for C-peptide ($P<0.05$) and a negative association between proinsulin concentrations and ISI composite values were observed in PCOS patients ($P<0.05$). Conclusions: Data suggest that in PCOS patients an elevated proinsulin concentration could reflect insulin resistance more than beta-cell dysfunction. However, the elevated concentration of proinsulin in these patients could also result from impaired beta-cell function resulting from intra-abdominal obesity independently of insulin resistance.

Eur. Cytokine Netw, 2003; 14(3): 128-33

Ex vivo lipopolysacharide (LPS)-induced TNF-α, IL-1β, IL6 and PGE2 secretion in whole blood from type 1 diabetes mellitus patients with or without aggressive periodontitis.

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Several studies have demonstrated that diabetes is a risk factor for developing periodontal disease, increasing its prevalence and severity. Furthermore, periodontitis may impair the metabolic control and adequate treatment of diabetic patients. LPS from Gram-negative bacteria penetrates the periodontal tissues and subsequently recruints and activates immunes cells. Progession to severe periodontitis with loss of supporting structures is mediated by several factors, including secretion of a broad spectrum of inflammatory and destructive mediators such as cytokines (TNF-α, IL-1β, and IL6), chemokines (IL-8) and prostaglandin E2 (PGE2).
The aim of this work is to investigate differences in the TNF-α, IL-1β, and IL6 expression an prostaglandin E2 (PGE2) realease in the blood from diabetic patients with and without aggressive periodontitis (AP) stimulated with lipopollysaccharide (LPS). For this purpose we recruited 29 type 1 Diabetes Mellitus (DM) patients, 14 with AP and 15 without AP. Fourteen healthy individuals formed the control group, for cytokine expression and PGE2 secretion, an ex vivo whole blood culture system was used. Cytokines and PGE2 were detected by commercial immunometric assays. A wide range of inter-individual variability in spontaneus and LPS-induced TNF-α, IL-1β, and IL6 levels in patient grups and controls was found. The mean of spontaneous and LPS-induced TNF-α, IL-1β, levels did not differ significantly ($p>0.5$) when patients were compared to control

individuals. Although not significant, the spontaneous TNF-α, IL-1β, and IL6 levels in the group of type 1 DM with AP were higher than in controls while diabetic patients without AP, these values were depressed in comparison with controls. In both groups of patients, the means of LPS-induced IL-6 levels were higher than controls but the differences observed were not significant (p=0.07). However, the LPS-induced PGE2 levels varied significantly when all groups were compared (p=0.007). The means of LPS-induced PGE2 levels for type 1 diabetic patients with AP (p=0.0009) and without AP (p=0.024) were significantly higher than the levels observed for healthy controls. Finally, we conclude that type 1 diabetic patients with or without AP did not express higher LPS-induced TNF-α, IL-1β, and IL6 levels than controls,. However, the PGE2 levels released were significantly higher than those detected in controls.

Keywords: TNF-α, IL-1β, and IL6. PGE2 diabetes.

Genética

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True mosaicism in a case of Williams syndrome.

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Williams syndrome is a neurodevelopmental disorder with multisystemic manifestations. Most patients (>96%) exhibit a common 1,5 Mb de novo heterozygous deletion in 7q11.23 that results from non-allelic homologous recombination between regional segmental duplications during meiosis. To our knowledge, mosaicism has never been reported.
We have studied a 5-year old Chilean patient with characteristic facial features, supravalvular aortic stenosis, gastroesophageal reflux, bilateral inguinal hernia, hoarse voice, severe psychomotor retardation, characteristic autistic features, besides global delay in language development and partial heterochromia of the left iris. Repeated FISH analyses on two independent blood samples showed the co-existence of cells with and without a heterozygous deletion of the ELN probe (deletion of 46% and 41% out of 80 and 39 metaphases, respectively). Typing of short tandem repeats on blood genomic DNA revealed biparental inheritance with a relative dosage reduction of the paternally inherited allele (47-51%) at HSB055XE5, ELN and D7S1870, while normal dosage ratios were found at D7S672 and D7S2518. Our data indicate the presence of somatic mosaicism in lymphocytes for the common WS deletion. Other tissues are currently being analysed. Contrary to expected, the phenotype of the patient is rather severe.
Proyecto Fondecyt 1010816

Congreso Brasilero de Genética Clínica 19 al 22 de junio, Porto Alegre, Brasil.

Las alteraciones cromosómicas encontradas en adenocarcinomas de vesícula biliar no representan amplificaciones del oncogen her 2 neu.

Sanz P, Pardo A, Castillo S, Smok G, Capetillo M, Nielsen E, Biagini L, Fodor M.

El adenocarcinoma de vesícula biliar representa la primera causa de muerte por tumor maligno en mujeres mayores de 50 años. Frecuentemente se diagnostica en etapas avanzadas en las que el pronóstico de sobrevida es malo. Se desconoce su mecanismo cromosómico y molecular de inicio, así como la secuencia de eventos que se producen durante su desarrollo. No hay marcadores citogenéticos ni moleculares diagnósticos ni pronósticos. En 30% de carcinoma invasivo de mama se evidencian amplificaciones del oncogen Her2/neu, por técnicas de inmunohistoquímica o de FISH, cuyo hallazgo positivo tiene un valor pronóstico y son un criterio de selección terapéutica. La proteína amplificada funciona como recptor transmembrana, similar al factor de crecimiento fibroblástico y su sobreexpresión resulta en una proliferación exacerbada. Esta proteína puede ser bloqueada con anticuerpos, Tranzumab o Herceptin, que constituye un tratamiento efectivo empleado en

estos cánceres, inhibiendo la proliferación celular en tejidos con sobreexpresión.

En estudios cromosómicos previos en adenocarcinomas de vesícula biliar, observamos la presencia de isocromosoma 17q, donde se localiza 2Her/neu, además de observar dobles minutas y cromosomas marcadores con aspecto de regiones homogeneamente coloreadas que podrían corresponder a amplificaciones de este oncogen, al igual que otros autores como Hecht y Gonunova. En base a estos hallazgos, se realizó estudio inmunohistoquímico en muestras de adenocarcinomas avanzados de vesícula biliar. La detección de la proteína amplificada con inmunohistoquímica se hizo en cortes de tejido incluídos en parafina, empleamos kit Hercep Test (IHQ-Dako), cuya sensibilidad es de 85-100%, la especificidad es de casi 100%. Se empleron criterios de inclusión establecidos.

Analizamos 20 casos y 20 controles. Se realizó análisis estadístico en Epinfo con un error alpha de 0,05, razón de sisparidad de 3, empleando test de Fisher.

El resultado fue no significativo, descartamos amplificaciones de Her2/neu en las muestras de adenocarcinoma avanzado.

Deben haber otros genes amplificados involucrados en esta neoplasia, lo cual debería ser estudiado por CGH y multiple FISDH para esclarecer su origen y trascendencia.

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Impact of wheat flour fortification with folic acid (FA) on the frequency of Neural Tube Defects (NTD) in Chile : preliminary results.

Cortés F, Hertrampf E, Mellado C, Castillo S, Erickson D.

Introduction: The protective effect of FA over NTD frequency is widely accepted. In Chile, starting January 2000, the Chilean Ministry of Health legislated to add FA to wheat flour to reduce the risk of NTD. This policy resulted in a mean FA additional supply of 427 ug/d. Serum folate and red cell folate increased significantly in fertile women after fortification.

Objective: To measure the impact of this fortification on the NTD frequency. Methods: All births, live births (LB) and stillbirths (SB) with birth weight > 500g of the 9 maternity hospitals of Santiago from 1999-2000 (pre-fortification) and 2001-2002 (post-fortification) are included, corresponding to 60.000 births/year. In each hospital, a contact professional (medical doctor or midwife) examines and registers each LB ans SB with NTD, then information is confirmed by the research team through different sources and registers. This information is monthly reviewed and rechecked periodically.

Results: The NTD rate for the pre-fortification period over a total of 120.636 newborns was 16,99/10.000 births (13,28/10.000 LB and 501,09/10.000 SB). The NTD rate for the post-fortification period (January 2001 – June 2002) in 88.358 births, was significantly reduced 41% to 10,07 (8,8/10.000 LB and 214,3/10.000 SB). For the pre-fortification period rates of anencephaly, encephalocele and spina bifida were 5,97; 2,49 and 8,54/10.000, and for the post-fortification period were 3,85; 1,7 and 4,53/10.000 respectively.

Conclusions: Fortification of wheat flour with FA in Chile is apparently effective in the reduction of NTD.

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Family with ODED (oculo-dento-esophageal-duodenal) syndrome

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The propositus (C.G.R.) is a 5-year-old boy seen initially for a major malformation (esophageal atresia) and his younger brother (B.G.R.) with mild developmental retardation and multiple congenital anomalies. Their parents are young and healthy and non consanguineous. In both pregnancies, there was no history of exposure to infectious agents, radiation, drugs or other known teratogens.

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Hemifacial myohyperplasia: an additional case.

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Hemifacial myohyperplasia is the term chosen by Lee et al (2001) to describe an uncommon manifestation leading to facial asymmetry, due to unilateral hyperplasia of the facial muscles (probably derivatives of the first and second branchial arches) with no evidence of hyperplasia of bone or other organ systems.

Three patients described by Lee et al (2001) and six by Staffenberg et al (1998) share hypertrophy and asymmetry of the facial muscles and presence of anomalous neck musculature with clinical characteristics that place them into a distinct syndrome.

We report on a 10-year-old boy who was derived to our Genetic Unit for establishing a diagnosis. He was the fourth child of young, healthy and non-consanguineous parents, without history of teratogenic exposure. Pregnancy and birth were uneventfull. Birth weight was 3.450 g and birth length was 49 cm, immediately right palpebral ptosis was noted and interpreted as a consequence of uterine compression. Anthropometric measures and psychomotor development have been normal.

The older son was born at 36 weeks of gestation by vaginal delivery. Pregnancy was complicated by partial disrruption of placenta at 3-4 months of gestation. Birth weight was 3.000 g and birth length 47,5 cm. An esophageal atresia with tracheoesophageal fistula was diagnosed at birth and repaired surgically, no other abnormalities were described at this time. Some associated pathologies with ambulatory management are gastroesophageal reflux in his first year; neumonias at age 6 months, 2 years and multiple respiratory infections during his third year of life. He has had 5 endoscopic surgical interventions because of reappearance of the tracheoesophageal fistula.

At age 5 his psychomotor development is normal. On physical examination he is 115,8 cm tall, weight 22.500 g, and head circumference 52 cm. He has long eyelashes, prominent ears and two frontal hairwhorls. He has a cavernous hemangiomata on the sacral area, around 2x3 cm. He has slight brachydactyly, particularly notorious in the distal falanges of his toes, with bilateral partial sindactyly of toes 2-3 and 3-4.

The younger son was born at 37 weeks of gestation by vaginal delivery. Pregnancy was complicated by partial disrruption of placenta at 3-4 months of gestation and premature delivery threat, ultrasonographic analysis were normal. Birth weight was 3.100 g, birth length 47,5 cm, CC 34 cm and Apgar 9-9. A duodenal diaphragma was diagnosed in the second portion of the duodenum and surgery done at 24 hours of life. He presented with bilateral club foot and multiple dysmorphias like blepharochimosis, epicantus, low nasal bridge, big ears, partial syndactyly of toes 2-3 and 3-4 with hypoplastic nails. A transfontanelar ultrasonography was normal, an ecocardiography diagnosed physiologic pulmonar stenosis of the newborn.

At age 20 months he has CC: 47,5 cm and brachycephaly with occipital flatness, and the already described facial dysmorphias. He shows a cavernomatous hemangioma on the right pectoral area, hernia of the white line and normal masculine genitalia. Equine position still remains on the left foot. He has slight psychomotor retardation. A caryotype shows a 47,XYY constitution.

ODED or Feingold syndrome was described in 1975. It is caracterized by short palpebral fissures,

esophageal/duodenal atresia, brachydactyly, syndactyly of toes 2/3 and 4/5 , clinodactyly of fingers, variable microcephaly, learning disability and autosomal dominant pattern of inheritance. Recently, Celli et al. 2000, showed that haploinsufficiency for a gene or genes in 2p23-p24 is associated with this syndromic esophageal atresia. Our patients suggest a recessive inheritance of a very unfrecuent and perhaps underdiagnosed condition.

American Journal of Medical Genetics, 2003, 121A : 41-46.

Beare-Stevenson Syndrome: two south american cases with FGFR2 analysis.

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We report two patients with Beare-Stevenson Syndrome. This syndrome presents craniosynostosis with or without clover-leaf skull, craniofacial anomalies, cutis gyrata, achantosis nigricans, prominent umbilical stump, furrowed palms and soles, genital and anal anomalies. Both female newborn patients presented at birth craniofacial anomalies, variable cutis gyrata in forehead and preauricular regions, prominent umbilical stump and anogenital anomalies. Furrowed palms and soles were also observed. The radiologic examination showed a cloverleaf-form craniosynostosis. Chromosomes were normal. They were born with respiratory distress and were connected to mechanical ventilation for ventilatory support. Both of them died in 50 days after birth due to secondary complications. The molecular analysis of this patients identified the mutation Tyr375Cys in the FGFR2 gene.

Ginecología

JSLS 2003 Jan-Mar; 7(1): 53-8.

Complications of operative gynecological laparoscopy.

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Objective: To assess the incidence and type of laparoscopic complications. Methods: A series of 2140 operative laparoscopies were reviewed in a retrospective study of patient records. The setting was a tertiary-care university hospital. Operative laparoscopy included minor procedures (minimal adhesiolysis, destruction of minimal endometriosis foci, ovarian biopsy, ovarian puncture, tubal sterilization), major laparoscopic surgery (extended adhesiolysis, tuboplasties, uterine suspension, treatment for ectopic pregnancy, salpingitis, ovarian cyst, moderate and severe endometriosis), and advanced laparoscopic surgery (hysterectomy, myomectomy, bladder neck suspension). Results: Two major vascular complications, 3 intestinal injuries, 1 anesthesiological complication, and 4 urinary tract injuries occurred. Two minor and 5 postoperative complications were noted. The overall complication rate was 17/2140 (0.79%). The major complication rate was 10/2140 (0.46%). Conclusions: This review is useful for helping surgeons reduce the risk of injuries and to inform patients about potential complications. These rates are similar to those that have been previously reported.

III Congress Inter American Division of the International Society of Hematology. Octubre 22-25, Santiago, Chile.

Recolección de progenitores hematopoyéticos de sangre periférica (PHSP) post quimioterapia, sincronizado con un corto periodo de G-CSF.

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Introduction: PBCP collection include chemotherapy administration followed by G-CSF from first day post-chemotherapy. Based on hematological recovery observed in the different chemotherapy protocols, we used G-CSF lately in the course of chemotherapy tryping to synchronize its use with the expected hematological recovery. By this protocol we avoid a prolonged use of G-CSF, reducing cost and mainting the efficiernсy of mobilization.

Pacients and methods: 34 patients were consecutively mobilized (33 hematological and 1 solid tumors) using diverse schemes of chemotherapy (ESHAP 15 pts, Cyclophosphamide (Cy) 3 gr/m2 9 pts, etoposide + Ara-C 8 pts, MINE 1 pts, hyper C-VAD 1 pt). We began with G-CSF (Neupogen 300 mcg) at the eight day post chemotherapy, with the exception of etoposdide + Ara-C started at day +14. The harvesting was made by large volume leukapheresis, starting the fifth day of G-CSF and repeated until we obtained the minimal dose for transplant (2,5 x 106 CD34/Kg).

Results: The average colllection was 6,4 x 106 CD34/Kg (rank 2-20). In 21/34 (62%) we collected more than 2,5 x 106 CD34/Kg in one apheresis. The average number of days of agranulocytosis during mobilization was days for ESHAP, 4.5 days for Cy and 14 days for etoposide+Ara-C. In all of them a recruitment of CD34(+) cell could be observed during leukapheresis equivalent to 2,9 times the CD34(+) quantitation pre-apheresis. Up to now, we have transplanted 25 patient, all of them with hematological recovery, RAN over 500/ul in average at day +10 (rank 8-14), platelets greater of 20.000/ul at day +11 (rank 8-21). The transplant-associated mortality was of 1/25 (4%) due to a Fournier gangrene.

Discussion: The use of G-CSF in the phase of hematological recovery allows not only an optimal CD-34 collection, but also permit to reduce cost and mainting a good efficiency of the procedures.

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Prophylaxis of Venous Thrombosis (VT) Associated with central Venous Catheter (CVC) with low molecular weight hepatin (LMWH) in Hematologic Malignancies.

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The incidence of VT in patients (pts) with cancer is high (37 to 66%) and its cause is multifactorial. Its prevention with warfarin an LMWH has diminished its frequency in solid tumors. There are few reports of pts with acute leukemia (AL) or other hematological malignances.

An open, prospective, aleatory study, with two branches, randomized in a 2:1 relation to receiving or not dalteparin (D) 5000 U sc daily during the first 7 days after insertion of a CVC was performed pts. older than 15 years requiring CVC insertion for a week or more, normal coagulation study platelet count higher than 100 x 10^3 mL were included. All the pts signed and informed consent. The results were analysed with X2 (CHI square).

39 pts with 58 catheter events were studied: 44 AL, 10 NHL and others. Median age was 42.8 years (range 15 to 71). Catheter triple lumen, made of polyurethane, 7Fr, in jugular position (42 pts) or subclavian position (16 pts) were used. Daily clinical signs and symptoms of thrombosis were evaluated, and Eco Doppler with a 7,5 MH_2 linear tromsducer (ATL 5000) was carried out on days 2 and 7. Almost all CVC events (57/58) were submitted to chemotherapy. Results: VT associated with CVC was demonstrated in 12% of the events (7/58) through eco-Doppler within the first week of CVC insertion

and all of them were asymptomatic 4/38 (10,5%) of pts. with D presented VT and 3/20 (15%) pf pts without prophylaxis developed VT (p=0.619). No pts presented CVC infection signs during the first week of follow-up. No relationship between CVC position (jugular of subclavian) and VT, neither with previous CVC insertion in the same venous location was observed. VT was more common in the AL pts, among which 6/7 presented VT with a total incidence of 13,6%. Conclusion: There are no significative differences between treated pts and the control group. VT is a frequent complication in AL pts with CVC being asymptomatic during the first week. It is suggested to study other factors as endothelial damage, cytokine liberation, activation via extrinsic pathway as well as appraise the use of higher D dose or its use before CVC insertion.

Infectología

J Clin Microbiol 2003;41:1617-22.

Analysis of molecular epidemiology of Chilean Salmonellas enterica serotype enteritidis isolates by pulsed-field gel electrophoresis and bacteriophage typing.

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Human Salmonella enterica serotype Enteritidis infections emerged in Chile in 1994. S. enterica serotype Enteritidis phage type 1 isolates predominated in the north, and phage type 4 isolates predominated in the central and southern regions. A study was planned to characterize this epidemic using the best discriminatory typing technique. Research involved 441 S. enterica serotype Enteritidis isolates, including clinical preepidemic samples (n = 74; 1975 to 1993) and epidemic (n = 199), food (n = 72), poultry (n = 57), and some Latin American (n = 39) isolates. The best method was selected based on a sample of preepidemic isolates, analyzing the discriminatory power (DP) obtained by phage typing and randomly amplified polymorphic DNA and pulsed-field gel electophoresis (PFGE) analysis. The highest DP was associated with BInI PFGE-bacteriophage typing analysis (0.993). A total of 38 BInI patterns (B patterns) were identified before the epidemic period, 19 since 1994, and only 4 in both periods. Two major clusters were identified by phylogenetic analysis, and the predominant B patterns clustered in the same branch. Combined analysis revealed that specific B pattern-phage type combinations (subtypes) disappeared before 1994, that different genotypes associated with S. enterica serotype Enteritidis phage type 4 had been observed since 1988, and that strain diversity increased before the expansion of S. enterica serotype Enteritidis in 1994. Predominant subtype B3-phage type 4 was associated with the central and southern regions, and subtype B38-phage type 1 was associated with the north ($P < 0.0001$). Food and poultry isolates matched the predominant S. enterica serotype Enteritidis subtypes, but isolates identified in neighboring countries (Peru and Bolivia) did not match S. enterica serotype Enteritidis subtypes identified in the north of Chile. The results of this work demonstrate that genetic diversity, replacement, and expansion of specific S. enterica serotype Enteritidis subtypes were associated with epidemic changes.

Scand J Infect Dis 2003;35: 892-3.

Unsuccessful treatment with voriconazole of a brain abscess due to Cladophialophora bantiana.

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Cladophialophora bantiana is a dematiaceous fungus, associated with brain abscess in normal or immunosuppressed patients. We report a case of CNS infection in this agent unsuccessfully treated by surgery and various antifungal compounds including high doses of voriconazole (6 mg/kg bid). No adverse effects related to this compound were observed.

Inmunología

IX European AIDS Conference, Polonia, Octubre 2003.

Primary resistance in HIV chilean patients:Genotypic Assay.

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Background: Highly active antiretroviral therapy (HAART) regimen change the natural history of HIV infected patients. Drug resistance is one of the most relevant problems of the treatment failure. The prevalence of drug resistance mutations detected in antiretroviral naive patients (primary resistance) has show differences in geografhic areas. Our aim is to establish a preliminary prevalence study of primary resistance on HIV Chileans patients.
Methods: 60 blood samples were collected from antiretroviral-naive chronically infected patients. The samples has been randomly selected from HIV population controlled in the northen area of Santiago, beetween November 2001 and December 2002. The genotypic analysis was performed by using the commercially available sequencing kit, TrueGene HIV-1 Genityping assay (Visible Genetics).
Results: The analized samples were 93,4% male (56/60) and 6,6% female (4/60). The average and median age were 36 years (23-54), 66% (40/60) were homosexual. CD4 T cell count average was 212 cells/ul (68-509) and viral load average was 124.190 copies/ml (6.100-800.000). A total of 7 mutations were identified in the reverse transcriptase or protease genes. No mutations associated with intermediate/high level resistance to NRTI, NNRTI or PI were found.
Secondary mutations were found in 28 patients (46,6%): the most frequent mutations were L10I, L63P and A71T/V.
Conclusion: This is the first study of primary resistance in HIV Chilean patients. Primary mutations associated with NRTI, NNRTI, or PI resistance were not found in antiretroviral-naive adults. Secondary mutations were identify in this group, which could contribute to resistance in the future.

XXII Congress of the European Academy of Allergology & Clinical Immunology, Paris 7 - 11 Junio 2003.

Prevalence of latex sensitizacion and allergy among operation room health care workers in Chile: preliminary results.

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Background: Health care workers (HCW) are high risk group for developing natural rubber latex (NRL) sensitizacion and allergy. There is no published prevalence data in our country. Some studies have shown a correlation between time in a frecquency of exposure to NRL gloves and sensitizacion but recent meta-analysis demonstrated there is no clear evidence for such an assumption.
Objective: The aim of this study was to determine the prevalence of NRL sensitization and allergy in a group of HCW at Hospital Clínico Universidad de Chile, and correlate it with years and frequency of NRL exposure.
Materials and Methods: Fifty nine HCW (17 anaesthesiologists, 5 suegeons, 17 nurses, 17 aides, and 3 medical students) were interviewed asking them for time of exposure, atopic diseases and latex-related allergy symptoms. They were skin with commercially available NRL extract (Leti. Spain), a 12-hour phosphate-buffered saline extract of latex examination gloves, and ammoniated latex (Madegom. Chile). Seven different NRL gloves brands were also tested by the prick-in-prick, method.
Results: The mean age was 35,5 years +/- 9. 61% were female (F) and 39% male (M). Total sensitization rate was 20,3% (n=12) (95% IC=11% - 32,8%), with no differences beetwen F (22,2%) and M (17,4%) (p=0,459). No one of the patients referred contact urticaria. In workplace, respiratory symptoms reached 10,2% of the patients, but were no cases in the sentized group. Sensitized patients to NRL, showed no differences in the autorrefered atopic diseases (58,3% and 55.3% respectively, p=0,557) and the mean of years at the workplace: 15 +/- 8,45 (years +/- DS) and 12,1 +/- 8,9 (years +/ - DS) respectively. We found an increase in the sensitization rate to NRL, from 12% in patients working less than 10 years, to 23% in the group bet-

ween 10 and 20 years and to 58% in those working more than 21 years. We did not found sensitizcion in the group who had more than 31 years of exposure (p=0,052). WWe found sensitizacion related with the weekly hour of exposure: 1-10 hours, 4,5% 11-20 hours, 18,2%; 21-30 hours, 50% and 31-40 hours, 25% (p=0,013). Discussion: Sesitization increased proportionally to the years and weekly hours wearing NLR gloves, but decreased with more than 31 years and 31 hours per week of exposure, perhaps indicating a tolerance mechanism.

Atopy and asthma: sensation characteristics in children with asthma in Santiago, Chile.

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Objective: The aim of this study was to determine the prevalence of atopic asthma, and analyse clinical characteristics of atopic and non-atopic asthma children. Our second aim was to determine the allergens, involved in sensitization. Material and Methods: From March 2001 to February 2002 four hundred and fifty nine phisician-diagnosed asthmatic children, aged between 2 and 14 years were enrolled. They were referred to the Pulmonology Section of a pediatric Universitary Hospital to performe a skin prick test (SPT). A standardized questinaire, including demographic, clinical and enviromental asthma related questions was completed. SPT with 37 allergens (indoor, outdoor and food allergens) was performed. Atopic asthma was defined as at least one positive SPT.

Results: Two hundred and seventy-nine asthmatic were males and 180 females (mean age 97.5, b 37.9 months). Athopy was found in 61% (n=221) with an increase in sensitization with the age (p<0.01). There was no difference between atopic asthma and non-atopic asthma in term of gender, type of birth delivery, breastfeeding, tobacco exposure ans parental atopy. Non-atopic asthmatics, started to wheeze before 6 month of age, with a higher frequency (33,8%) than atopic asthmatic children (23.5%), P=0.037. Previous history of rhinitis and dermatitis was a risk factor for sensitization (OR:1.5,95% IC:1-2,24). The most prevalent allergens found, were house dust mites (53,1%), followed by pollens (36%) and foods (10%). Children with mattresses older than 2 years, had a higher risk for Dermathohgoides sensitization (OR: 1.7, 95& IC: 1-2,82) and exposure to dog dander was a risk factor to dog sensitization (OR: 2.6, 95% IC: 0,98-8,03).

Conclusion: Sixty one percent of our asthmatic children was atopic, similarly than previously reported in our city. This prevalence increased with age. We found parental atopy, breastfeeding and tabacco exposure not realated to the developement of sensitization in this group. We corroborated that expossure is a key factor in specific sensitization, as show by the relationship between house dust mite exposure (mattress age) and sensitization to Dermatophagoides and dog exposure and sensitization.

Laboratorio

Neuroendocrinology 2003; 77(4): 273-81.

Thyrotropin-releasing hormone as a mediator of the central autonomic pathway controlling ovarian function.

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We studied the effect of thyrotropin-releasing hormone (TRH) applied centrally on the sympathetic activity of the ovary in female rats. Intracerebroventricular (i.c.v.) administration of a dose of 25 ng/kg weight produced an increase in noradrenaline (NA) content at the ovary after 5 days of hormone administration. However, higher doses in a range up to 500 ng/kg weight decreased NA content at the ovary. At the celiac ganglia (where the cell bodies of sympathetic neurons projecting to the ovary originate) there was an accumulation of NA in spite of a decrease in tyrosine hydroxylase activity (T-OH). After cold exposure, opposite effects on T-OH activity and no effects on NA in ganglia and in ovary were obtained. Besides, i.v. injection of TRH only induced a decrease in ovarian NA. In contrast to the increase in T(3) plasma levels obtained after the cold-stress procedure, none of the i.c.v. doses of TRH used produced changes in T(3) plasma levels, strongly suggesting that the effect on sympathetic activity is mediated by a central effect of TRH acting as a putative activator of ovarian sympathetic nerves. Copyright 2003 S. Karger AG, Basel

XIV Congress of the Interamerican Division of the International Society of Haematology, Santiago, 22 - 25 Octubre 2003.

Características clínicas y epidemiológicas de pacientes hospitalizados con indicación de terapia anticoagulante oral en el Hospital Clínico de la Universidad de Chile.

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Introducción: Los pacientes con terapia anticoagulante oral (TAC oral) controlados en el policlínico del Hospital Clínico de la Universidad de Chile han aumentado desde 4.925 pacientes en el año 1998 a 9.115 en el 2002. Para conocer sus características epidemiológicas, se estudió a todos los pacientes hospitalizados que tuvieron indicación de inicio de TAC oral, durante un año a partir del 1 de mayo de 2002.
Material y Método: Se analizaron los antecedentes clínicos y de evaluación del TAC oral. Durante ese período, se inició tratamiento con acenocumarol, a 181 hombres y 171 mujeres, entre los 14 y 88 años. Para el análisis estadístico se utilizaron los promedios, desviaciones estándar (DS) y coeficientes de correlación (R2).
Resultados: Durante un año, se inició TAC oral a 352 pacientes, de ellos 17 tuvieron más de una hospitalización y uno falleció durante ella. A 326 pacientes (92,6%), se indicó un INR = 2 a 3 y a 26 (7,4%) se indicó un INR = 2,5 a 3,5. En 103 pacientes (29,3%) la causal del TAC oral fue Trombosis Venosa Profunda, en 83 (23,6%) la indicación fue fibrilación auricular, 44 (12,5%) pacientes presentaron tromboembolismo pulmonar y 44 (12,5%) tuvieron un reemplazo valvular cardíaco. Al analizar la estabilidad del tratamiento con acenocumarol, no hay relación entre el logro del INR esperado y la precocidad de inicio del tratamiento ni tampoco con el número de controles post hospitalización. Los resultados obtenidos hace necesario evaluar el reemplazo del anticoagulante oral, actualmente usado de rutina en los pacientes hospitalizados en el Hospital Clínico Universidad de Chile.

		Cell dyn	Sysmex	R 2
Leucocitos		7.162 ± 3.101	7.260 ± 3.128	0,991
Hematocrito (%)	37,9 ± 5,4	39,7 ± 5,5	0,920	
Glóbulos rojos		4,33 ± 0,6	4,58 ± 0,7	0,963

XIV Congreso Interamerican division of the international society of Hematology

Estudio comparativo de 2 contadores hematológicos y fórmula diferencial manual.

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Introducción: Los equipos contadores Hematológicos Cell Dyn 3700 y Sysmex 1800i procesan muestras de sangre total, entregando los parámetros de WBC (Leucocitos), RBC (eritrocitos), PLT (plaquetas) y cinco poblaciones celulares en un sistema cerrado. Material y Método: Se utilizaron muestras de sangre de pacientes adultos hombres y mujeres recolectadas en tubos vacutainer. Se analizaron 294 muestras en sistema cerrado con cargador automático, con lector de código de barras. Las muestra fueron procesadas en los 2 equipos y la determinación de las subpoblaciones fue comparada con la formula realizada con microscopía.

Resultados: Al comparar los resultados obtenidos en ambos equipos para leucocitos, hematocrito y glóbulos rojos se obtuvo los siguientes resultados:

En el caso de las fórmulas diferenciales se analizó los informados por los equipos respecto de la microscopía. Por ej. los neutrófilos (%) se obtuvo para el Cell dyn 60,3 ± 13,1, en el Sysmex 60,2 ± 13,0 y la microscopía 60,9 ± 12,5.

Conclusiones: Los resultados obtenidos entre ambos contadores hematológicos son comparables entre sí y respecto de la microscopía. El cargador automático del Cell Dyn 3700 procesa 60 muestras por hora y el del equipo Sysmex 1800i procesa 80 muestras por hora.

Nefrología

J Cardiovasc Pharmacol 2003 Oct; 42: 453-61.

Implications of oxidative stress and homocysteine in the pathophysiology of essential hypertension.

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The present review examines the clinical and experimental data to support the view that homocysteine and oxidative stress, two alternative risk factors of vascular disease, may play a role in the pathogenesis of primary or essential hypertension. Although the precise mechanism of this disease has not been elucidated, it may be related to impairment of vascular endothelial and smooth muscle cell function. Thus, the occurrence of endothelial dysfunction could contribute to alterations of the endothelium-dependent vasomotor regulation. Hyperhomocysteinemia limits the bioavailability of nitric oxide, increases oxidative stress, stimulates the proliferation of vascular smooth muscle cells, and alters the elastic properties of the vascular wall. The link between oxidative stress and hyperhomocysteinemia is also biologically plausible, because homocysteine promotes oxidant injury to the endothelium. Cumulated evidence suggests that the diminution of oxidative stress with antioxidants or the correction of hyperhomocysteinemia with vitamins-B plus folic acid, could be useful as an adjuvant therapy for essential hypertension. Further studies involving long-term trials could help to assess the tolerability and efficacy of the use of these therapeutic agents.

J Clin Pharmacol 2003 Dec; 43: 1299-306.

Homocysteine and essential hypertension.

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The authors examine the available clinical and experimental data supporting the view that homocysteine, an alternative risk factor of cardiovascular disease, may play a role in the pathogenesis of essential hypertension. The mechanism of this disease has not been elucidated, but it may be related to impairment of vascular endothelial and smooth muscle cell function. Therefore, the occurrence of endothelial dysfunction could contribute to alterations of the endothelium-dependent vasomotor regulation. Elevated homocysteinemia diminishes the vasodilation by nitric oxide, increases oxidative stress, stimulates the proliferation of vascular smooth muscle cells, and alters the elastic properties of the vascular wall. Thus, homocysteine contributes to elevate the blood pressure. Also it is known that elevated plasma levels of homocysteine could lead to oxidant injury to the endothelium. The correction of elevated homocysteinemia by administration of vitamins B12 and B6 plus folic acid, could be a useful adjuvant therapy of hypertension. However, further controlled randomized trials are necessary to establish the efficacy and tolerability of these potentially therapeutic agents.

Nefrologia 2003; 23: 47-52.

Usefulness of thoracic radiography after insertion of transitory catheters for hemodialysis

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A chest X-ray has been routinely used to evaluate possible complications of a catheter installed for hemodialysis. The objective of the present study was to evaluate the utility of routine chest X-ray to detect complications derived from the installation of temporary catheters through a jugular vein access. We studied prospectively 95 successive jugular catheters for hemodialysis. After installation the operator answered a questionnaire that asked for details of the procedure and his opinion of the utility of a chest X-ray to detect a complication in each particular case. A chest X-ray was done in every patient and analyzed blindly. There were 17 minor complications: 7 arterial punctures, 5 neck hematomas and 5 malpositions of catheters. No major complications were found. Sixty per cent of the catheters that required three or more punctures had a complication vs only 10% of the ones that required two or less puncture ($p < 0.05$). In five occasions the catheters were malpositioned, in four of these cases a complication was suspected. The wire guide was twisted in all of these cases. The procedure was considered of medium or high difficulty in four of the five malpositioned catheters, in contrast a medium or highly difficult case was considered only in 13 of the 90 well positioned catheters ($p < 0.05$). The time employed for the catheters installation was significantly higher for the malpositioned catheters. In 29.5% of the cases the operator considered a chest X-ray necessary, 2/3 of the cases did not have a well founded clinical suspicion of complication. We conclude that routine chest X-ray after installation of a jugular catheter for hemodialysis has a low diagnostic value for the detection of complications derived from the procedure and should be ordered only when clinical features suggest a complication.

Neurología

Neuroepidemiology 2003; 22: 339-44.

Alcohol and hemorrhagic stroke in Santiago, Chile. A case-control study.

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Background and purpose: Hemorrhagic stroke (HS) is a major cause of disability and death worldwide. There is a dearth of information on HS from geographically defined populations in Latin America. In this study we assessed the importance of alcohol consumption as a risk factor for HS in Chile. Methods: Case-control study in Santiago, Chile, of 140 consecutive patients with CT-confirmed HS, matched by sex and age with 140 hospital controls. Alcohol consumption was measured in grams (ethanol) per week, using a questionnaire administered to the patients or caregivers or both. We defined four categories of alcohol consumption: non-drinkers (0.0 g/week), light (0.1-115 g/week), moderate (116-402.5 g/week) and heavy drinkers (>402.5 g/week). Other variables measured included diabetes mellitus (DM), cigarette smoking, arterial hypertension, liver disease and chronic use of nonsteroidal anti-inflammatory drugs (NSAID). Statistical analysis was performed with STATA 6.0 software. Results: A total of 280 subjects with a mean age of 65.5 years were studied over a 3-year period, 122 men (43.5%) and 158 women (56.5%). Alcohol intake was 394.1 g/week among cases and 174.5 g/week in controls (p=0.01). The following odds ratios (OR) with 95% confidence intervals (CI) were found: hypertension 4.89 (2.86-10.3) and chronic use of NSAID 3.44 (2.15-12.9). Using conditional logistic regression analysis high alcohol intake was found to have a statistically significant OR of 4.47 (CI 1.14-17.2). Conclusions: In Chile, a high alcohol intake (>402.5 g/week) increased more than 4 times the risk of HS and remained a significant risk factor for HS after controlling for hypertension, cigarette smoking, liver disease, blood cholesterol levels, and chronic use of NSAID. The risk was higher in younger patients (<65 years of age).

Am J Physiol Cell Physiol 2003; 285: 119-28.

SH oxidation coordinates subunits of rat brain ryanodine receptor channels activated by calcium and ATP.

Bull R, Marengo JJ, Finkelstein JP, Behrens MI, Alvarez O.
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We have reported that ryanodine receptor (RyR) channels display three different responses to cytoplasmic free Ca2+ concentration ([Ca2+]) depending on their redox state (Marengo JJ, Hidalgo C, and Bull R. Biophys J 74: 1263-1277, 1998), with low, moderate, and high maximal fractional open times (Po). Activation by ATP of single RyR channels from rat brain cortex was tested in planar lipid bilayers with 10 or 0.1 microM cytoplasmic [Ca2+]. At 10 microM [Ca2+], low-Po channels presented lower apparent affinity to activation by ATP [[ATP] for half-maximal activation (KaATP) = 422 microM] than moderate-Po channels (KaATP = 82 microM). Oxidation of low-Po channels with thimerosal or 2,2'-dithiodipyridine (DTDP) gave rise to moderate-Po channels and decreased KaATP from 422 to 82 microM. At 0.1 microM cytoplasmic [Ca2+], ATP induced an almost negligible activation of low-Po channels. After oxidation to high-Po behavior, activation by ATP was markedly increased. Noise analysis of single-channel fluctuations of low-Po channels at 10 microM [Ca2+] plus ATP revealed the presence of subconductance states, suggesting a conduction mechanism that involves four independent subchannels. On oxidation the subchannels opened and closed in a concerted mode.

Nuclear

Alasbimn Journal 5: July 2003: Number 21(S).

Myocardial Perfusion Versus Left Ventricular Wall Motion one Month Post Acute Myocardial Infarction, After Successful Thrombolysis. Analysis by two Independent Observers.

Massardo T [1], Olea E, Coll C, Velásquez C, Quintana JC, González P, Allende I.
Nuclear Medicine, Clinical hospitals, Universidad de Chile and Catholic University of Chile.

AIM: The aim was to evaluate myocardial perfusion and ventricular function in post acute myocardial infarction (AMI) patients after thrombolysis and also, to determine the report criteria for future cooperative task.
Material and Method: 60 patients (mean age 56 ± 11; 87% male) with recent AMI (no prior MI) and successful thrombolysis. In all of them rest perfusion with Sestamibi (7 ± 1 days post AMI) and rest MUGA (30 ± 1,5 days post AMI) were performed. A GE Startcam and ADAC Genesis cameras were used. A semi-quantitative analysis of 17 segments was used (ASNC criteria). The analysis was done by two independent and blind observers in all 1020 segments. Left ventricular ejection fraction (EF) was automatically obtained. Perfusion defect were correlated with abnormal wall motion areas (See table).
Results: Mean EF was 38,7 ± 15%; in 35% of patients < 30%. Interobserver agreement for a normal or abnormal study was 98% for perfusion and 93% for wall motion. The agreement by segments for extension was 86% in perfusion and 68% in wall motion and for severity was 81% in perfusion and 74% in wall motion. The involved segment/patient ratio in perfusion was 9,3 ± 4 (extension 54,6 ± 24%) and mean severity 2,5 ± 0,6; for wall motion was 10.7 ± 5 (extension 63,1 ± 29,7%) and mean severity 2,3 ± 0,8. The wall motion/perfusion agreement was 45,29% (Cohen Kappa 0.45).
Conclusion: A good inter observer agreement was obtained (discrepancies were due to small AMI reperfused). Being both techniques not totally comparable, the agreement segment by segment was acceptable between rest perfusion and MUGA studies. These indicate global normal segments or same degree of abnormality in the initial perfusion and wall motion one month after a successful reperfusion.

Motion Perfusion	Normal (0)	Mild hipokinesia (1)	Moderate hypokinesia (2)	Severe hipokinesia (3)	Akinesia or dyskinesia(4)
Normal (0)	274	75	51	41	26
Mild defect (1)	38	15	32	8	7
Moderate defect (2)	33	17	47	37	18
Severe defect (3)	21	6	34	46	46
Absance (4)	10	6	21	36	80

Preliminary Experience in Positron Emission Tomography with dedicated PET.

Jofré MJ, Massardo T, Humeres P, Canessa J, González P, Sierralta P, Galaz R.

We present our preliminary experience with Positron Emission Tomography, using Fluor 18- deoxyglucose, in a Siemens HR+ equipment.
Materials and Methods: F18-FDG was obtained from the cyclotron IBA Cyclone 18/9 installed in the Chilean Agency of Nuclear Energy. We studied 39 subjects (mean age: 51.5 y.o.; 12 were males); 36 of them with known oncological disease, 2 healthy volunteers and 1 patient with acute myocardial infarction (MI). We obtained a total of 52 scans (37 whole body, 6 brain and 3 cardiac studies and also 6 inferior extremities scans). Mean blood glucose level was 93 mg/dl (range 69-139). Mean F18-FDG injected dose was 11.7 mCi. PET studies were analyzed by 4 independent observers visually and calculating standardized uptake value (SUV).

Results: In 9/39 oncological patients, PET scans were normal or without metastasis/ recurrent disease. In 27/36 patients abnormal focal uptake was observed as evidence of recurrence or metastasis and in two other patients a second tumor was found (proven as rectal and breast cancer). In the healthy control scans PET did not shown abnormalities and in the cardiac patient, viability was found in the inferior wall (concordant with the location of a recent MI).
Conclusion: We confirm that metabolic imaging with F18-FDG is very helpful in the evaluation of oncological patients and improves patient management.

Post-stress functional behavior in gated SPECT using Tc99m Sestamibi and i.v. Dipyridamole in patients with and without known coronary artery disease.

Massardo T, Anzotaegui W, González P, Miranda K, Carmona A, Rodríguez JL, Garcés N.

Introduction: Normal subjects show increase in left ejection fraction (EF) with exercise. In patients with coronary artery disease (CAD), induced myocardial ischemia and abnormal regional contraction may produce significant EF decrease during stress. Dipyridamole (DIP) produce variable effect on EF in healthy population; in CAD patients the induced ischemia with this vasodilator also could decrease systolic function. By the other hand, post-stress EF obtained with gated SPECT represents a different value than the obtained at maximal stress and it should be avoided a delay in the acquisition. The goal of this work was to evaluate post-DIP and rest systolic function in patients with and without known CAD. Material and Methods: Ninety patients were studied prospectively in 4 months including finally only 69 of them (mean age 66±11 y.o.; 51% males). In 75% of the cases the test was performed to rule out CAD and the rest have known disease. Thirteen percent presented also other cardiovascular disease an 3/69 prior myocardial infarction. A Tc99m Sestamibi single day protocol was performed with DIP infusion (0.56 mg/kg in 4 min). Images were acquired with a dual head Siemens ECAM system, 30 min post DIP and 45-60 min post Sestamibi at rest (camera heads in 90 degrees angle by anterior). All patients received milk, 10-15 min post injection. Cedars QPS and QGS program was applied. Perfusion images were interpreted independent of functional results. End diastolic and end systolic volumes (EDV and ESV) and EF values were analyzed as well as reversibility obtained automatically (SDS). Results: Twenty-one out of 90 patients were excluded (23%) due to difficulty for searching the left cavity border, principally by hepatic or colonic activity, mostly post stress in patients with inferior defects. In the total group EF was similar in both phases ($p > 0.05$); EF at rest was 63,1+20,1 % , EF post DIP was 63,4 +19,5% and delta EF was 0,29+6,36%. The only difference found was in left ventricular EF at rest and post DIP, between the groups with normal or abnormal perfusion scan. However, EF variation did not show significant difference ,as well as transient dilation, in the groups with and without: a) known CAD [n:19 and 50]; b) ischemia in the perfusion scan [n: 26 and 43]; c) reversibility as SDS <5 or />5 [n: 49 and 20]; and d) normal perfusion scan [n: 36 and 33].
Conclusion: The analysis of left ventricular functional changes early post stress with DIP using automatic program with Sestamibi did not present discriminative value for ischemia at individual basis. It is possible than vasodilators are not as adequate as exercise for this object due to the important hepatic radiopharmaceutical excretion in the initial period post DIP infusion. It is necessary to increase the sample to confirm this data.
Microvascular Angina Detection Using Cardiac Single Positron Emission Tomography (Spet). Left ventricular ejection fraction and volumes at rest with gated SPECT in patients with normal perfusion scan. Correspondencia entre los 17 segmentos del ventrículo izquierdo y cada una de las arterias coronarias. Reducción del tiempo de estancia en urgencias y del número de ingresos de los pacientes con dolor torácico y ECG no diagnóstico en los que se practica un gated SPET de perfusión miocárdica. El SPECT de Perfusión Miocárdica Como Método de Screening para Enfermedad Coronaria en Pacientes con Arteriopatía Periférica. El SPECT de Perfusión Miocárdica en el Infarto de Miocardio sin Onda Q. Post-stress functional behavior in gated SPECT using Tc99m Sestamibi and i.v. Dipyridamole

in patients with and without known coronary artery disease. Valor Diagnóstico de la Gamagrafía Spect/ Tetrofosmin-Tc99m/Sincronizado para la Identificación de Enfermedad Arterial Coronaria en Mujeres: Estudio Comparativo con Talio-201 Radiación endovascular con ^{188}Re para la prevención de restenosis post-angioplastia: resultados preliminares. Valores de Fracción de Eyección y Volúmenes Ventriculares en Reposo con Spect Gatillado en Sujetos con Imágenes de Perfusión Coronaria Normal. Myocardial Perfusion Versus Left Ventricular Wall Motion one Month Post Acute Myocardial Infarction, After Successful Thrombolysis. Analysis by two Independent Observers.

Normal iodine (131I) thyroideal uptake value at 2 and 24 h in adults from Santiago, Chile and La Paz, Bolivia.

Miranda K [1], Massardo T, González P, Araya V, Olaechea M, Carmona A, Jiménez B, Sánchez C, Padilla P, Alay R.
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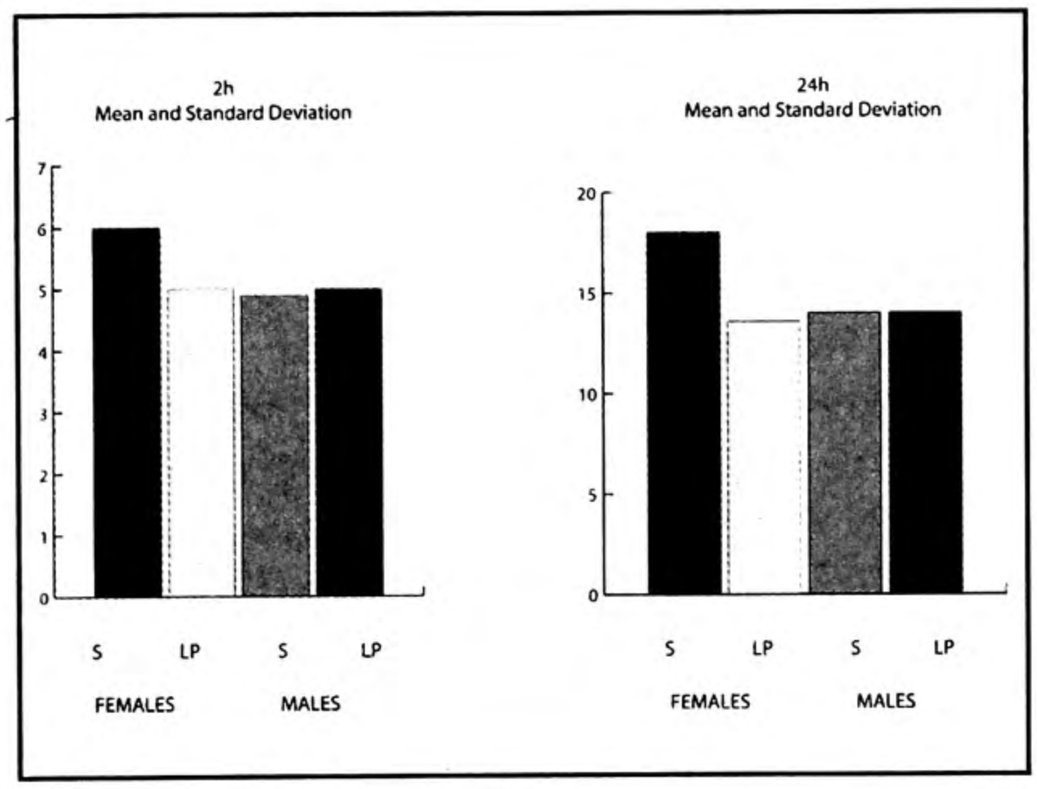
Introduction: Iodine uptake value is helpful in the study of thyroidal diseases allowing the evaluation of intraglandular metabolism. There are extrathyroidal factors able to modify the uptake, including diet supplies.
Objective: It was to obtain local normal values for 131I thyroid uptake in normal volunteers by gender, comparing the cities of Santiago (S), Chile and La Paz (LP), Bolivia (regions with different location and altitude: 400 vs. 3600 m over the sea level. Both countries have salt iodination.
Material and Methods: A questionnaire (hormones intake, iodine compounds or pregnancy) and specific clinical exam was applied to assure absence of endocrinological disease. TSH and Anti-TPO levels were measured by CLIA and RIA methods. A total of 113 patients from both sex were included, mean age 51 y.o. (range:20-70, homogeneously distributed). The uptake measurement was performed according to IAEA standards. The dose was 5-10 uCi

Total (both sexs)	Group	Santiago (n:87)	La Paz (n:26)	p
2h		5.41+1.76	5.12+1.01	
		[2.32-11.35]	[3.3-7.0]	ns
24 h		16.32+5.06	14.6+3.26	
		[6.45-33.41]	[7.1-21.8]	ns

oral and a Nuclear Chicago Thyrad was used twice at 2 and 24 h in both centers.
Results: they were compared with student t test. There was no significant difference in thyroid iodine uptake by region, age or gender at 2 and 24 h ($p > 0.05$). Results in percentage as mean + SD were as shown in the following figures and table:
Conclusion: Factors as gender, ethnical origin or geographic iodine intake does not influence the of thyroideal iodine uptake values.



Left ventricular ejection fraction and volumes at rest with gated SPECT in patients with normal perfusion scan.

Carmona A, González P, Húmeres P, Anzoategui W, Massardo T, Pennaroli U, Videla J, Otarola S.
Clínica Santa María - Santiago Chile and Universidad de Chile Clinical Hospital. Programa OIEA at Universidad de Chile.

Introduction: Functional data could improve the evaluation of gated SPECT when it is calculated simultaneously. The main goal of this abstract was to measure the left ventricular ejection fraction (EF) and the ventricular volumes in patients without known coronary artery disease (CAD) in order to have reference values at rest.
Material and methods: It was a retrospective study of 12 months including 67 patients, 44 from Clinica Santa Maria (CSM) (gammacamera ADAC and Pegasys computer) and 23 from the Universidad de Chile Hospital (gammacamera Siemens e-CAM). Software QGS – QPS, Cedars-Sinai was used in both centers. Thirty-two patients performed Bruce exercise protocol in treadmill and 35 pharmacological stress with Dipyridamole, but only resting images were analyzed. The mean age of the total group corresponded to62 y.o in males and 61 y.o. in females; there was no difference in age or body mass index between both centers.
Results: As seen in the Table:
EF values at Universidad de Chile ranged from 55-96% with a mean of 76 ± 14%, significantly lower than those of CSM ($p < 0.0003$).
Conclusions: Every nuclear medicine center should establish its own reference values according to equipments and software available. It is confirmed that left ventricular EF values are higher for women with lower ventricular volumes. There is not significant differences in hypertensive patients and non hypertensive patients from both centers.

Eur J Nucl Med Mo Imaging 2003 Mar; 30: 479-80.

Quantitative and visual characterization of gastric images obtained with FDG-F18 PET in patients without gastroesophageal carcinomas.

Massardo T, Coll C, Redondo F, Miranda k.

Introduction: The normal stomach presents diverse uptake intensity with FDG PET images tomography and it could be difficult to differentiate from local neoplastic disease. Objective: It was to evaluate the stomach characteristics and organ variants in patients with other non gastric or esophageal neoplasm. Quantitave Standarized Uptake Value (SUV) and visual analysis were employed. Methods: Twenty-four patients were retrospectively studied at CETIR Center (mean age: 58 ±16 years, 54% males). Blood glucose level was within normal limits in all patients (mean: 95.3 mg/dl). FDG doses corresponded to 8.4 ±1.3 mCi. Images at 45 min post FDG injection were performed with PET GE Advance equipment with standard whole body acquisition. Visual analysis was employed for describing the shape, position and uptake. Maximal (MAX) and average (AVE) SUV was measured using standard circular gastric and hepatic right lobe ROI.

Mean+ SD [Range]	Total	Females*	Males*	Hypertensive	Normotensive
EF (%)	63 ± 7	68 ± 7	59 ± 5	65 ± 7	61 ± 7
	[49-82]	[56-82]	[49-69]	[53-78]	[49-82]
EDV (ml)	81 ± 22	65 ± 15	93 ± 19	74 ± 15	84 ± 24
	[38-132]	[38-97]	[60-132]	[49-102]	[38-132]
ESV (ml)	32 ± 13	23 ± 9	38 ± 11	27 ± 10	34 ± 13
	[7-59]	[7-43]	[21-59]	[11-43]	[7-59]
n	44	19	25	15	20

*$p < 0.00005$

Results: All cases presented gastric uptake at visual analysis; 13 presented greater uptake than liver and it was lower in 3 patients. The most frequent shape was ovoid and longer in the anteroposterior axis in the transaxial and sagital slices and circular in the coronal slices. In 15 cases the gastric walls and in 3 the whole stomach were clearly seen. In stomach MAX SUV ranged between 1.595 and 7.199 g/ml and AVE SUV between 1.036 and 6.582. Mean SUV corresponded to 3.63±1.31 for 1 MAX and 2.82±1.14 for AVE, respectively. In liver the MAX SUV ranged between 1.02 and 5.334 and AVE between 0.539 and 3.68, their means corresponded to 3.38±1.14 and 2.08±0.71, respectively. There was significant difference between hepatic stomach and AVE SUV ($p < 0.005$). The mean ratio SUV AVE gastric / SUV AVE in liver was 1.46±0.8; in all cases it was < 4.23 and in 29% it was < 1. The same mean ratio for MAX SUV was always < 2.77 and in 54% it was < 1.

Conclusion: In oncological patients gastric metabolic activity was greater than liver activity and this feature was more common than expected. Uptake severity and extension present wide variation. These results may be helpful for PET imaging interpretation, mainly in those patients with gastroesophageal carcinomas.

Med Sci Monit 2003 Aug; 9: CR363-8

Could the [14C]urea breath test be proposed as a 'gold standard' for detection of Helicobacter pylori infection?.

Gonzalez P, Galleguillos C, Massardo T, Rivera M, Morales A, Smok G, Moyano L, Pimentel C, Alay R, Otarola S.
Nuclear Medicine, Gastroenterology and Pathology Centers, University of Chile Clinical Hospital, Santiago, Chile.
pgonzalez@ns.hospital.uchile.cl

Background: The urea breath test (UBT) with a microdose of [14C] is a non-invasive and simple method for the assessment of gastric infection by Helicobacter pylori. The aim of this study was to compare the [14C]UBT with invasive methods widely used for assessment of H. pylori gastric infection, including histology with hematoxylin-eosin staining, the gastric smear technique using Giemsa staining, and the biopsy urease test. Material and Methods: We evaluated patients referred to our clinic for elective upper gastrointestinal endoscopy excluding those on antibiotics and/or bismuth during the previous 4 weeks, patients on H+ blockers or H2 antihistamines during the previous 7 days, pregnant women, and patients who had undergone gastric surgery or had bleeding disorders. Eighty-nine patients ranging in age from 18-75 years were included in the final study population, 61 women and 28 men (mean age: 43(15 years). RESULTS: When histology alone was considered as the reference standard, sensitivity for the [14 C]UBT was 94%, with a specificity of 37%; when the Giemsa technique, sensitivity was 95%, and specificity 35%; and when the biopsy urease test, sensitivity was 94% and specificity 45%. With two or more invasive techniques together considered as the reference standard, the [14C]UBT had a sensitivity of 95%, with a specificity of 44%. Conclusions: [14C]UBT is an objective and reproducible technique, capable of sampling the whole gastric mucosa. It shows high sensitivity, but low specificity, which could be explained by limited gastric sampling plus subjective interpretation in the invasive techniques that are currently used as gold standard.

Eur J Nucl Med Mol Imaging 2003 Mar; 30: 479-80.

Analysis of contuining education and scientific activities at the 2002 WFNMB meeting, Santiago, Chile.

Massardo T, Coll Claudia, Redondo F, Miranda,
(Local Scientific Commtee, 2002 WFNM/ALASBIMN) Santiago, Chile, October 2002.

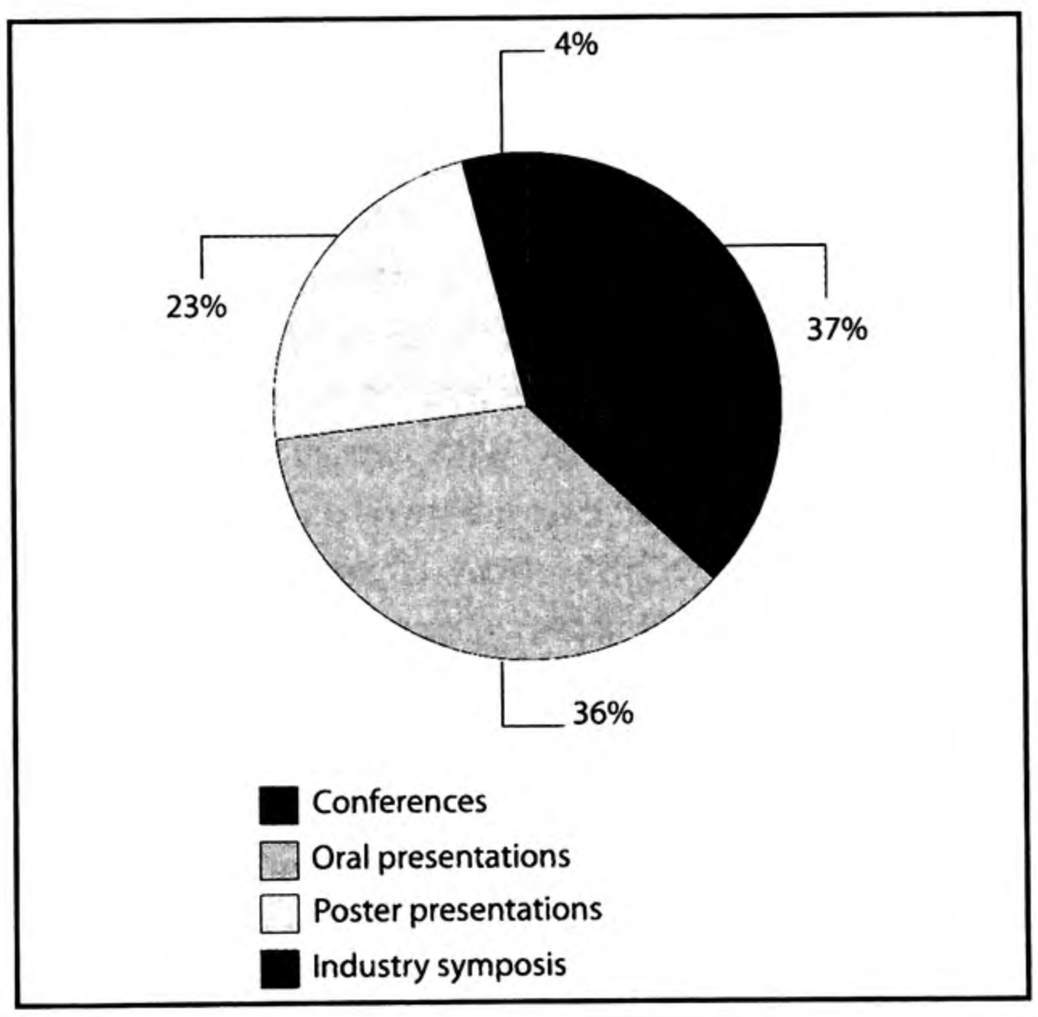
The 8th World Federation of Nuclear Medicine and Biology (WFNMB) Meeting was held in conjunction with the 18th Association of Latin American Societies of Biology and Nuclear Medicine meeting fron September 29 to October 4, 2002 in Santiago, Chile, at the Casapiedra Convention Center.

In this short report, we present an overview of the WFNMB meeting, using the information provided by the moderators of the various scientific activities.

We are not aware of provision of such information fron previous similar meetings, and we consider that it may be interesting and helpful for the organization of future WFNMB congresses.

1. About 1,500 participants were registered, and 147 of them were speakers during the meeting.

2. At the beginning of the event, Profesor Patricio González, Secretary General WFNMB and Scientific Chairman of the Congress, presented the academic program, including the American Medical Association (AMA) credits available during the WFNMB Congress, coordinated by Profesor Ismael Mena, our International Scientific Chairman. He also introduced the Scientific Commitee, with Dr. Edwaldo Camargo as ALASBIMN representative, and thanked the lecturers from all aver the world, the members of the scientific committees, the moderators, and the reviewers of abstracts. He explained the diverse academic activities of the meeting, including the industry symposia. Finally, he mentioned that abstracts which achieved the best scores during the blind review process would have their titles highlighted in the congress book, in recognition of their quality.



Distribution (percentage of total time) of scheduled scientific activities at the 2002 WFNMI ALASBIMN meeting.

3. The AMA, General Technologists, Physicists and Radiopharmaceutical Scientific Activities at the meeting were perfomed in accordance with the program. Sessions each lasted 90 minutes and were held over 6 days (20 AMA, 24 General Program, 4 Radiopharmacy, 10 Technologists, and 9 Physicists sessions). Each included two to four lectures. Moderators of these sessions ensured that the scheduled time was always respected and that there was interesting discussions at the end of most of them. Only in two cases was lecture delivered by a speaker not lised in the program. Two short lectures could not be delivered, in one case because the speaker did not show up and in the other for unexpected personal reasons.

4. Plenary and Special Sessions were well attended and were conducted in accordance with the program. The talks given by Professors Henry Wagner Jr., Peter Ell, and Thomas Behr were of a very high scientific standard (state of the art in the specialty).

5. The distribution of scientific activities at the meeting is show in the figure. Approximately 700 free communications were selected for the meeting. Sixty-one percent of them (425 abstracts) were selected for the oral presentation, and the remainder (272) as poster.

6. The 68 oral free comunication sessions were held simultaneously in up to six hall over 5 days. Only in 12 sessions were all scheduled abstracts presented. In total, 102 abstracts were not presented, corresponding to 24% of the total. Of these, a la large proportion were from Asia (30% from China

and 18% fron India). Eight percent were for Italy, and the rest were from a variety of regions, specially Latin America, eastern Europe, and other areas of Asia.

7. The 44 poster sessions were held at midday in two halls, over the course of three days. In 34% of the poster sessions (15/44), all selected posters were displayed. Of the 272 posters selected, 49 were not displayed (18%).

Of the non displayed posters, 36% were fron Asia (mainly China, Taiwan and Japan), 32% from Latin America (mostly Brazil, and then Argentina) and 25% fron Europe (mainly Germany, Yugoslavia, and Italy).

8. Approximately 35% of the authors did not discuss their papers during the programmed poster sessions.

9. All abstracts are available electronically via the ALASBIMN Journal site: www.alabismnjournal.cl

The above data reflect the current reality in the world, and can probably be plained by political, economic, and geographic difficulties. Firts, some groups in North America have certain relutance to travel beyond their borders.

Second, several countries, mainly in Latin America, Asia, and eastern Europe, have significant budget problems and not all WFNMB members are able to afford the cost of meetings without help from their institutions or the industry. Furthe more, some of those who would be interested in participating live very far from the selected meeting venue, and long trips are not always well accepted.

In order to avoid or reduce the absence of authors of free presentation at future meetings, we suggest that a minimun free should be charged upon submission of the abstracts, this representing a percentage of the registration fee. Another possibility, wich we do not want to apply currently, is to withdraw the non-presented abstracts from our electronic publication.

As regards the organization of the meeting, we would like to offer our sincere thanks to all the speakers and moderators, who ensured that the event was a big success. Gratitude is especially due to MARINA Cabrejas, Ph.D., for coordinating the physicists, technologists, and radiopharmacy programs. We also thank all the participants for their interest in the meeting.

We hope that the next WFNMB Meeting, in Seoul, Korea in 2006, will enjoy similar levels of teamwork and participation.

Were are grateful to Professor Gonzalez for reviewing and providing data.

Nucl Med Commun 2003 Nov; 24 (11): 1155-65

An assessment of wall motion, perfusion and glucose metabolism in recent myocardial infarction: a comparison in patients with and without revascularization.

González P, Massardo T, Coll C, Redondo F, Yovanovich J, Jofre J, Chamorro H, Humeres P, Sierralta P, Ramirez A, Kunstmann S, Lopez H, Aramburu I, Brugere S.

Summary: The aim of this study was to compare the extent and severity of wall motion abnormalities, perfusion and glucose metabolism, in recent myocardial infarction in patients with and without revascularization. Forty-nine patients were studied (82% men; mean age 58 years) by using echocardiography, 201Tl single photon emission computed tomography (SPECT) rest and redistribution, and 2-[18F]fluoro-2-deoxy-D-glucose (18F-FDG) SPECT at a mean of 9.2 days (range, 1-24 days) after myocardial infarction. Twenty-seven of the 49 patients underwent revascularization while the other 22 received medical therapy before echocardiography and studies using radionuclides. A contrast angiogram was obtained for each patient. A follow-up echocardiogram at 3 months was obtained for 44 patients. Images were read blindly, using a 17 segment model, with semi-quantitative analysis. In the whole group, the extent of hypokinesia was 15%+/-14 (mean+/-SD); the extent of mild defects was determined as 5%+/-6 by using 201Tl at rest, 6%+/-9 by using 201Tl redistribution, and 4%+/-6 by using 18F-FDG (P<0.0005, echocardiogram/radionuclides). Echocardiography showed that the extent of akinesia-dyskinesia was 16%+/-18 in revascularized patients and 28%+/-18 in non-revascularized patients (P=0.017). With regard to moderate and severe defects, 201Tl rest showed 19%+/-16 and 28%+/-17, respectively (P=0.047); 201Tl redistribu-

tion 17%+/-15 and 26%+/-15, respectively (P=0.043); and 18F-FDG 17%+/-13 and 24%+/-15, respectively (NS). In echocardiography, the extent of hypokinetic segments decreased from 16%+/-15 at baseline to 10%+/-11 at 3 months (P=0.045), in revascularized patients. It is concluded that, in recent myocardial infarction, hypokinesia extent on echocardiogram is greater than mild perfusion or metabolic defect extent, reflecting stunning and so the use of radionuclide techniques appear more accurate for defining the extent of myocardial infarction. Non-revascularized patients showed a significantly greater extent of akinesia-dyskinesia and moderate-severe perfusion defects than did revascularized patients, which can be considered a result of therapy. It is suggested that 201Tl rest perfusion be used for the assessment of myocardial infarction soon after revascularization.

Obstetricia

13th World Congress on Ultrasound in Obstetrics and Gynecology, 31 August- 4 September 2003, Paris - France.

Biochemical markers and uterine artery Doppler as predictors of complicated pregnancies.

Parra M, Rodrigo R, Barja P, Bosco C, Fernández, Muñoz H, Matamala P.
Faculty of Medicine, and Hospital Clinico Universidad de Chile,Chile.

Objective: The purpose of this study was to evaluate whether systematic screening with an uterine artery Doppler and maternal serum biochemical markers of oxidate strees and endothelial dysfunction predict efficiently preeclampsia and fetal growth restriction (FGR) in an unselected population.
Methods: This prospective case control study involved 623 asymptomatic pregnant women seanned at 22-25 weeks. The subjects were women who were delivered either due to preeclampsia ar FGR and who were enrolled routinely between 22-25 weeks.
Doppler of the uterine artery waveform and measurement of maternal 8 serum and red blood cell markers of oxidative strees and endothetial dysfunction were performed.
Results: There was a 43% and 18% increased of uterine artery resistance in women who developed either preeclampsia of FGR compared to control pregnancies, respectively. A multivariate analysis showed that mean PI uterine artery Doppler is useful as predictor of complicated pregnancies. In addition, uric acid and F-2 isoprostane levels were significantly higher in 'patients destined to develop preeclampsia (3.6 mg/dl* and 27+15.4, respectively; *p<0.05), than in those who did not developed adverse outcome (2.83 mg/dl and 23.1+11.5 pg/ml, respectively).
Conclusions: This study showed that uterine artery Doppler as a screening test is a good predictor of preeclamsia and FGR, although the measurement of some markers of oxidative strees and endothelial dysfunction, such as uric acid and F-2 isoprostane levels, may prove also useful in the selective prediction of complicated pregnancies.
Supported by Fondecyt N° 1020080.

XVII Congreso FIGO, Santiago 2-7 Noviembre 2003.

Uterine artery doopler and biochemical markers of oxidative stress and endothetial dysfunction as predictors of preeclampsia and fetal growth Restriction: Preliminary results.

Parra R, Rodrigo R, Barja O, Bosco C, Fernández V, Muñoz H, Matamala P.
Departament of Obstetrics and Gynecology, University of Chile, Santiago Chile.

Objective: The purpose of this study was to evaluate wheter systematic screening with a uterine artery Doppler and maternal serum biochemical markers of oxidate strees and endothetial dysfunction predict efficiently preeclampsia and fetal growth (FGR) in an unselected population.
Methods: This preliminary result of prospective case control study involving 623 asymptomatic pregnant womwn at 22-25 weeks from April to December 2002. The subjects were women to were delivered either due to preeclampia or intrauterine growth restriction and who were enrolled routinely between

22 to 25 weeks. Coppler assessment of the uterine artery waveform and measurement of maternal 8 serum and red blood cell markers of oxidate stree and endothelial dysfunction were performed.
Results: Uterine artery median PI performed at 22-25 week´s gestation was significantly increased in women who developed aither preeclampsia of FGR compared to control pregnancies (1.39 and 1.12 vs 0.95, respectively; $p<0.001$) and was a best predictor of preeclampsia I this study. However, uric acid and F-2 isoprostane levels were higher in patients destined to develop preeclampsia ($n=14$; median 3.6 mg/dl* and 27.1 $\pm$ 15.4, respectively;* $p<0.05$), than in those who did not developed adverse outcome at follow up ($n=52$; median 2.83 mg/dl and 23.1 $\pm$ 11.5 pg/ml, respectively).
Conclusion: This preliminary study showed that uterine artery Doppler as screening thest is the best predictor of preeclampsia and FGR, although the measurement of some markers of oxidative stress and endothelial dysfunction, such as uric acid and F-2 isoprotane levels may prove useful in the selective prediction of those conditions.
Supported by Fondecyt N° 1020080.

13th Congress on Ultrasound in Obstetrics and Gynecology, 31 August - 4 September 2003, París, France

Ultrasound reference ranges for fetal nasal bone in Chilean population

Larrea V*, Merino D+, Sepúlveda E+, Barrera C+, Matamala O+, Pedraza D+, Parra M+.
Chile and + Hospital Clinico Universidad de Chile, Chile.

Objective: The absence of nasal bone (NB) has been noted in trimomy 21 at 11 to 14 weeks gestation, but it is also known that this ultrasound marker differ from different races. The aim of this study was to establish the reference ranges throughout gestation and to evaluate its value for screening for chromosomal defects in a Chilean population.
Method: From june 2000 to may 2002, the fetal profile was examined to visualize the NB by standarized technique. Normal nasal bone reference ranges generated using a cross-sectional data on 400 consecutive singleton pregnancy bettween 11 to 40 weeks gestation.
Results: NB measurement was performed in 42.5 fetuses. NB was absent in 2 fetuses (0.5%), which both had Down Syndrome (DS).
There were 5 cases with chromosomal abnormalities, being 4 DS. There was a significant positive correlation with increasing gestational age ($r=0,68$; $p<0.001$). Expected NB length increased from 3,3 mm at 12 weeks to 11,4 mm at 40 weeks. The were 2/4 Down Syndrome (50%) with absent nasal bone, the other two cases with present NB had NB length within normal ranges for gestation (6 mm at 2,3 weeks and 9 mm at 3.5 weeks).
Conclusion: Our results demonstrate that it is possible to measure fetal NB size between 11 to 40 week gestation. Absence of NB may be indicative of DS. Further studies may be necessary to evaluate the role of NB length as a screening test for chromosomal abnormalities at different gestational ages.

XVIII Congreso FIGO, Santiago, 2-7 Noviembre.

Assessment of a screening program for adverse perinatal outcome using transvaginal uterine artery Doppler between 22 and 25 week´s gestation in an unselected chilean population.

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Departament of Obstetricts and Gynecology, University of Chile Santiago, Chile.

Objective: The purpose of this study was to evaluate the clinical value of the uterine artery color Doppler at 23 week´s gestation in predicting adverse perinatal outcomes in unselected population.
Methods: Uterine artery Doppler assessment was carried out at 22-25 week´s gestation in 1350 consecutive singleton pregnancies women attending routine antenatal care in a University Hospital in Chile. The mean pulsatility index was calculated and the predictive value of an average pulsatility index above 95th centiles in the detection of poor outcome was determined.
Results: Transvaginal color Doppler examination was performed in 1350 consecutive singleton pregnancies and completed outcome information was obtained in 1110 (83%) pregnancies. The median value was 1.02 and the 95th centile was 1,57. Poor outcome, defined as preeclampsia, fetal growth restriction (FGR), abruption placenta and preterm delivery before 34 weeks, ocurred in 143 (12.9%) pregnant women. Yhe incidence of preeclampsia anf FGR was 4.6% 5.2%, respectively. The sensitivity of the mean pulsatility index above 95th centile for poor outcome was 26%, and for preeclampsia was 33% Although, there were few cases with adverse outcome born before 35 weeks in our series (20 cases with just 6 preeclamptic pregnancies), the respective sensitivities for total adverse outcome and preeclampsia requiring delivery before 34 weeks was 45% (9out of 20 cases) and 67% (4 out of 6 cases), respectively.
Conclusions: Transvaginal uterine artery Doppler using as a screening test between 22-25 weeks identifies most of the pregnant women who developed severe adverse perinatal outcomes before 34 weeks of gestation. Supported by Fondecyt N° 1020080.

Screening of spontaneous preterm delivery by assessment of cervical length in an unselected chilean population.

Matamala P, Muñoz H, Valdivia J, Sepúlveda E, Jiménez P, Uriz A, Parra M.
Departament of Obstetrics and Gynecologic, University of Chile, Santiago, Chile.

Objective: To assess the ability of cervical length meassurement in a Chilean population as a predictor of spontaneous preterm birth in an unselected population.
Methods: This was a prospective study involving 1342 asymptomatic women with a singleton pregnancies attending for routine antenatal care at the University if Chile Hospital who underwent satandardized transvaginal scan at 22-25 weeks for evaluation of cervical length as a screening test for spontaneous preterm delivery. The mean cervical loenght was calculated and lengths were compared between groups that delivery at term and prematurely, this being as two groups, delivery before 35 and delivery 35-37 weeks of gestation. The sensitivity, specificity and positive and negative predictive value were calculated for delivering at different gestational ages.
Results: The mean gestational age at cervival assessment was 23 weeks. The rate of spontaneous delivery before 35 and 37 week`s gestation were 1.97% and 5.5% respectively. The mean cervical length at 23 weeks were 36.5 $\pm$ 5.7 mm. The cervical length was significantly shorter in the group that has preterm delivery before 35 week´s gestation than in wich had either a term and 35-37 weeks deliveries (median 30.5 mm vs 37 and 36 mm, respectively; p=< 0.001). Using a cut-off point of cervical length of 27 mm (5th centile(the sensitivity for delivering before 35 and 37 week´s gestation was 31.8% and 18% respectively.
Conclusion: The risk of preterm delivery is inversely correlated with cervical length ant routine transvaginal evaluation of the cervix perfomed between 22-25 weeks of gestation may help to identify patients at risk of preterm delivery.
Supported by Fetal Medicine Foundation.

Is there asociation between increased NT and ductus venosous assessment at 11 to 14 weeks gestation?

Puga M, Muñoz H, Valdés E, Barrera C, Villa S, Jiménez P, Parra M.
Departament of Obstetricts and Gynecology, University of Chile, Santiago, Chile.

Objectives: The pathophysiological mechanism of and enlarged nuchal translucency (NT) are no well know, but temporary cardiac dysfunction at early gestation has been suggested. Changes in ductus venosous (DV) blood flow verlocities have been reported in some chronosomal abnormal fetuses with enlarged NT. The aim of this study was to evaluate the role of DV blood flow assessment at 11-14 weeks of gestation in predicting adverse perinatal outcome.
Methods: Doppler flow measurements of the ductus venous were prospectively assessed in the 196 consecutive fetuses at the time of NT scan from june 2000 to May. Pulsatility Vein index (IPV) for the DV was calculated.
Results: The pregnancy aoutcome was available in 144 (75%) pregnancies. A chromosomal abnornality was found in 2 cases (1.4%) and there was aldo a fetus with Apert syndrome. IPV was above the 95th centile (1.37) in 5 cases (3.4%), which were most of them (4/5) associated with increased NT and adverse perinatal outcome. There was also a positive correlation between NT and DV ($r=0.071$: $p<0.001$).
Conclusion: Our results suggest that the evaluation of the IPV of DV at 11-14 weeks gestation is significantly related with increased NT and for such association is also an useful tool for screening of chromosomal abnormalities and a maker of abnormal perinatal outcome within the group with normal karyotype.

Fetal gender determination by ultrasound between 11 to 14 weeks gestation in a chilean population.

Pardes V, Puga M, Matamala P, Sepúlveda E, Pedraza D, Valdés S, Parra M.
Fetal Medicine Unit, University of Chile Hospital, Santos Dumont, Chile.

Objective: The aim of this study was to assess the feasibility of fetal stidied in 268 singleton pregnancies. An ultrasound examination was carried out routinely at 11-14 weeks and the fetal sex was identified in the transverse and sagital planes. The fetal gender was defined as male if the angle of the genital tubercle to horizontal line was greater than 30 degrees and female when the genital tbercle was parallel to the horizontal line. Maternal body mass index (BMI) was calculated and the fetal sex was confirmed at birth.
Results: The fetal gender determination increased with gestational age from 72.1% at 11 weeks, to 87.3% at 12 weeks, and to 96.3% at 13 weeks. Male fetuses were correctly assessed in 97.3% of the total cases and there were no significant changes with respect to gestional age. Female gender was successfully determined in 82.3% of babies and rhe ability of the operator to assing fetal sex improved with gestational age (64.7% of cases at 11 weeks and 94.0% at 13 weeks). There was a positive correlation between BMI and fetal gender assigned, being wrongly assigned in 6.8% of slim mother and 22.5% of obese women.
Conclusion: The determination of fetal gender by ultrasound between 11 to 14 weeks provided accurate prediction of the fetal sex. There was also significant improvement in the identificacion of the fetal gender as the gestional age advancing, wich may be explained by the embriologycal development of the external genitalia. This study has also show that one of the explanations of wrongly assigned fetal gender may be due to maternal obesity. Early determination of fetal gender could be of clinical value in cases of a positive family history of X-linked disorders, helping in making diagnosis of chorionicity in twin pregnancies and for social needs.

13th World Congress on Ultrasound, París, France.

Endothelial dysfunction is correlated with preeclampsia and fetal growth.

Parra M[1], Rodrigo R, Barja P, Bosco C, Fernández V, Muñoz H, Matamala P.
Faculty of Medicne, Chile and Hospital clinico Universidad de Chile, Chile.

Objective: Ther aim of this study was to evaluate endothelial dysfunction and oxidate streess parameters in complicated pregnancies. PAI-1 / PAI-2 ratio, known to be reduced in pathological pregnances, was taken as endothelial dysfunction index.
Methods: This study involved 53 pregnancies with preeclampsia, fetal growth restriction preterm deliveries and healthy control groups. Levels PAI-1 / PAI-2 ratio were determined in maternal plasma immediately after delivery. In addition morphological characteristics of placenta were assessed.
Results: There was a two-fold increased of PAI-1 / PAI-2 ratio in preeclamptic pregnancies compared to control group. This parameter was negatively correlated wiyh either gestational age and fetal growth in all analysed pregnancies (r= (-) 0.63 and (-) 0.70; $p<0.05$). Placental trophoblast of pathological pregnancies showed an increased extend of apoptosis compared to normal placentae.
Conclusion: These data sggest that associated with fetal size, gestational age delivery and placental damage.
Supported by Fondecyt N° 1020080.

Implementation of nuchal translucency screening in the detection of major congenital structural defects and chromosomal abnormalities in Chilean population.

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Hospital Clinico Universidad de Chile.

Objective: Increased nuchal translucency performed between 11 to 14 weeks of gestation is associated with high incidence of fetal chromosomal defects, structural abnormalities and generic síndromes. The aim of this study was to avaluate the outcome of babies with increased nuchal translucency.
Methods: 950 women with singleton pregnancies were seanned berween 11 to 14 week´s gestation as a screening test for chromosomal abnormalities and major congenital structural defects during two years two at the Fetal Medicine Unit, Universaty of Chile Hospital (2000-2002). Follow up of the outcome of most of the patients were carried out. The sensitivity, specificity, positive and negative predictive value for the detection of fetal detects of increased nuchal translucency (above 95 and 99th centiles) were determined.
Results: The pregnancy y outcome was available in 758 cases (80%)
The were 18 (2.3%) spontaneous abortions or intrauterine death. In the 740 survivors, 16 (2.1%) had structural or chromosomal abnormalities. The detection rate of having a pregnancy with fetal structural defects or chromosomal abnormalities in the group with nuchal translucency above 95th centile was 63%; for chromosomal abnormalities the sensitivity was 75%. There was also a positive correlation between increased nuchal translucency and higher incidence of chromosomal or structural abnormalities.
Conclusion: This study confirms the previous findings on the role of the increased nuchal translucency test in the early detection of chromosomal abnormalities, structural defects or genetic syndrome.
Supported by fetal medicine foundation.

Medicina Fetal

Asociation of increased nuchal translucency and ductus venosous assessment beetwen at 11 to 14 weeks of gestation.

Muñoz H, Puga M, Valdés E, Matamala P, Sepúlveda, Parra M.
Hospital Clinico Universidad de Chile, Chile.

Objectives: The pathophysiological mechanism of and enlarged nuchal translucency (NT) is no well know, but temporary cardiac dysfunction at early gestation has been suggested. Changes in ductus venosous (DV) blood flow verlocities have been reported in some chromosomal abnormal fetuses with enlarged NT. The aim of this study was to evaluate the role of DV blood flow assessment at 11-14 weeks of gestation in predicting adverse perinatal outcome.
Methods: Doppler flow measurements of the ductus venous were prospectively assessed in the 196 consecutive fetuses at the time of NT scan from june 2000 to May. Pulsatility Vein index (IPV) for the DV was calculated.
Results: The pregnancy outcome was available in 144 (75%) pregnancies. A chromosomal abnormality was found in 2 cases (1.4%) and there was aldo a fetus with Apert syndrome. IPV was above the 95th centile (1.37) in 5 cases (3.4%), which were most of them (4/5) associated with increased NT and adverse perinatal outcome. There was also a positive correlation between NT and DV ($r=0.71$: $p<0.001$).
Conclusion: Our results suggest that the evaluation of the IPV of DV at 11-14 weeks gestation is significantly related with increased NT and for such association is also an useful tool for screening of chromosomal abnormalities and a maker of abnormal perinatal outcome within the group with normal karyotype.

BJOC 2003; 109: 297-301

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

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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. Desing: 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.

XVII Congreso FIGO, Santiago 2-7 Noviembre.

Strippining membranes at therm: safe and effective method to reduce the incidence of spontaneus labor after 41 weeks.

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Departament of Obstetrics and Gynecology, Clinical Hospital, Universidad de Chile, Santiago Chile.

Objective: To determine whether weekly sweeping or stripping membranes beginning at 38 weeks could safely reduce the spontaneus labour rate after 41 weeks.
Methods: One hundred eigth antenatal low-risk patient with firm gestional dates were randomized to either a treatment or control group. Control subjects receivd gentle cervico-vaginal exam each week to assess. Bishop scores, whereas the treatment group also underwent weekly stripping of membranes beginning at 38 weeks. The primary outcome was the spontaneous labour rate before 41 weeks. Secondary outcomes included maternal and neonatal morbidity. The data were analyzed for statiscal differences using x2, Fisher exact test, Student t test and Wilcoxson rank-sum test.
Results: The subjects were demographically similar bettween the groups. Women who received treatment had fewer deliveries after 41 weeks than those in the control group (5 v/s 14, $p<0,05$). Maternal-foetal complications were similar in both groups.
Conclusions: Membrane stripping was safe and was associated with a decreased incidence of deliveries after 41 weeks.

Ultrasound Obstet Gynecol 2003 Feb; 21:170-3.

Comparison of color Doppler uterine artery indices in a population at high risk for adverse outcome at 24 weeks' gestation.

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

Objective: To compare uterine artery Doppler velocity and impedance indices in the presence and absence of uterine artery waveform notches, in the prediction of adverse pregnancy outcome in high-risk women. Methods: One hundred and fifty-seven women identified at Doppler screening as being at 'high risk' underwent a further uterine artery Doppler assessment at 24 weeks' gestation. Pulsatility and resistance indices and minimum, time averaged and time averaged maximum velocities were measured, and the presence of bilateral notches noted. Adverse outcomes were pre-eclampsia, birth weight less than the tenth centile, placental abruption and intrauterine death. The best cut-off for each parameter was assessed by univariate logistic regression, and the comparative performance of the screening parameters was assessed using kappa values. RESULTS: The best performing index in the presence of bilateral notches was mean resistance index, for a cut-off of 0.67, giving a kappa value of 0.65. Mean pulsatility index and lowest pulsatility index performed similarly well, both with kappa values of 0.58. All velocity indices apart from lowest minimum velocity had kappa values of < 0.4. When indices were analyzed, irrespective of notch status, mean resistance and mean pulsatility indices performed similarly, with kappa values of 0.49 and 0.46, respectively; mean minimum velocity had a kappa value of 0.4. Conclusions: In a high-risk population, uterine artery Doppler mean resistance indices perform better than do velocity indices in the prediction of adverse pregnancy outcome, irrespective of notch status.

Ultrasound Obstet Gynecol 2003 Sep; 22: 233-9.

Randomized controlled trial using low-dose aspirin in the prevention of pre-eclampsia in women with abnormal uterine artery Doppler at 23 weeks' gestation.

Yu CK, Papageorghiou AT, Parra M, Palma Dias R, Nicolaides KH; Fetal Medicine Foundation Second Trimester Screening Group.
Harris Birthright Research Centre for Fetal Medicine, King's College Hospital Medical School, London, UK.

Objective: Pre-eclampsia, which is a major cause of perinatal and maternal morbidity and mortality, is thought to be due to impaired perfusion of the placenta. There is contradictory evidence that the administration of low-dose aspirin may provide effective prophylaxis against the subsequent development of pre-eclampsia. In this study we tested the hypothesis that in women identified as being at high-risk for pre-eclampsia, because of impaired flow in the uterine arteries, the prophylactic use of low-dose aspirin from 23 weeks of gestation can reduce the incidence of pre-eclampsia. METHODS: We used color and pulsed Doppler to measure the flow in the uterine arteries in 19,950 singleton pregnancies at 22-24 weeks of gestation. Those women exhibiting increased impedance were recruited into a randomized study of aspirin 150 mg per day or placebo. We compared the two groups for the incidence of pre-eclampsia and the other consequences of impaired placentation. RESULTS: The screening study identified 844 women (4.2%) as being at high risk of uteroplacental insufficiency. After exclusion and refusal, 560 women were randomly allocated to aspirin 150 mg or placebo per day until 36 weeks' gestation. There were no significant differences between the aspirin and placebo groups in either the incidence of pre-eclampsia (18% vs. 19%, P = 0.6) or pre-eclampsia requiring delivery below 34 weeks (6% vs. 8%, P = 0.36). Furthermore, the administration of aspirin did not significantly alter the incidence of preterm delivery (24% vs. 27%, P = 0.46), birth weight below the 5th centile (22% vs. 24%, P = 0.4), perinatal death (3% vs. 1%, P = 0.33) or placental abruption (4% vs. 2%, P = 0.12). Conclusion: In pregnancies with impaired placentation, as demonstrated by increased impedance to flow in the uterine arteries, the daily administration of 150 mg aspirin after 23 weeks of gestation does not prevent the subsequent development of pre-eclampsia.

Oncología

ASCO Annual Meeting, May 31 - June 3, Chicago, Ilinois.

Docetaxel (D), Cisplatin, 5 fluorrouracil compared to cisplatin (C) and 5-fluorouracil (F) for chemotherapy-naïve patients with metastatic or locally recurrent, unresectable gastric carcinoma (MGC): interim results of a randomized phase III trial (V325).

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Background: MGC is incurable resulting in a median survival time ranging from 6-9 months. DCF is an active regimen against MGC and was selected by an Independent Data Monitoring Committee (IDMC) as the test arm based on the phase II randomized portion of V324. Methods: Chemotherapy-naïve patients with MGC were randomized to either D 75 mg/m_2 d 1, C 75 mg/m_2 d 1, and F 750 mg/m_2/d c.i. d 1-5 q 3 w or C 100 mg/m_2 d 1 and F 1000 mg/m_2 d c.i. d 1-5 q 4 w. Eligibility included histologically proven metastatic or locally unresectable gastric or gastroesophageal junction adenocarcinoma and measurable or evaluable disease. Biased-coin randomization was used to stratify for institution, liver metastases, prior gastrectomy, weight loss, and measurability. Tumor assessments were independently reviewed and the IDMC scrutinzed the study. Time to progression (TTP) was the

primary endpoint and overall survival (OS) was the major secondary endpoint. Results: 443/460 patients were randomized by Nov. 2002. Results on 232 patients (115/117 in DCF/CF) are presented based on a planned interim analysis. 88% of patients are eligible. Among treated patients (96%), the median age was 54 years; primary was in the gastric body (68%), and 98% had metastatic cancer. TTP was statistically superior (threshold = 0.0036) for DCF (5.2 months) compared to CF (3.7 months), hazard ratio (HR) 1.704. Response rate to DCF (39%) was statiscally superior to that of CF (23%), p=0.012. The median OS was 10.2 months for DCF, and 8.5 months for CF, HR 1.505 (NS, threshold=0.0053). Grade 3 / 4 AEs were reported in 82% and 81% of patients on DCF and CF, respectively. Death rate from all causes within 30 days of last infusion was 11.7% and 8.0%. Conclusion: DCF resulted in significantly longer TTP and higher response rate than CF. DCF may emerge as the standard for treatment of advanced gastric or gastroesophageal junction adenocarcinoma. Analysis on 460 patients will be presented.

Relationship between Gallbladder cancer (GBC) and cancer background of relatives.

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Gallbladder cancer is one of the neoplastic death causes in Chile Affecting mainly women older than 50 years. Its frequency increases with age, being most common in people in their 70 decade. The etiology of this disease is still unknown. As GBC is common in Amerindian people, there might be familial-genetic factors in its origin. The aim of this study was to detect a relationship between GBC and familial-genetic factors. A study of cases and controls was designed. The cases were patients suffering GBC diagnosed and /or treated between January 1995 and December 2000. The control patients were older that 30 years, cholecystectomized, with a negative post-surgical diagnosis for GBC from January to March 2001. The study was performed in the Clinical Hospital of the Universidad de Chile. Data collection was obtained from clinical records and/or phone questions to relatives of the patient (in cases of death or other reasons) or to the patient himself. The Chi-square method was used for statistical analyses. The study comprised 183 patients; 76 cases with a mean age of 59 (33-80) and 107 controls with a mean age of 47.7 (30-73). The percentages of females were 68.7 and 72 for case and control patients respectively. In first-line relatives, cancer background was found in 33 cases (44%) and in 21 controls (20%). These differences were statistically significant (X^2=12,23, f.d. =1, p=0.001). In second-line relatives, cancer background was collected from 289 case patients and 60 controls. Cancer background was found in 41% case patients and in 21% controls. The differences were not statistically significant (X^2=3,76, f.d. =1, p=0.052). Results permit to conclude that there is relationship between Gallbladder cancer and the cancer background of first-line relatives but not in second-line relatives. However, further studies are necessary to determine whether this relationship is due to genetic or environmental factors.

Pediatría

Antimicrobial Agents and Chemotherapy 2003; 47: 3179-86

High-Dose Azithromycin versus High-Dose Amoxicillin-Clavulanate for Treatment of Childen with Recurrent or Persistent Acute Otitis Media.

Arrieta A, Arguedas A, Fernandez P, Block S, Emperanza P, Vargas S, Erhardt W, De Caprariis P, Rothermel C.
Childrens's Hospital of Orange Conty, Orange, California, Neeman-ICIC, San José, Costa Rica; Hospital Clínico Universidad de Chile, Otomed-Servicio Otorrinolaringología, and Grupo de Estudios Clinicos, Facultad de Medicina Universidad de Chile, Santiago, Chile; Kentucky Pediatric Research, Bardstown, Kentucky; and Pfizer Inc, New York, New York.
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Infants and young children, especially those in day care, are at risk for recurrent or persistent acute otitis media (OAM). There are no data on oral alternatives de high-dose amoxicillin-clavulanate for treating OAM in these high-risk patients. In this double-blind, double-dummy multicenter clinical trial, we compared a novel, high-dose azithromycin regimen with high-dose amoxicillin-clavulanate for treatment of children with recurrent or persistent AOM. Three hundred four children were randomized; 300 received either high-dose azithromycin (20 mg/kg of body weight once a day for 3 days) or high-dose amoxicillin-clavulanate (90 mg/kg divided twice a day for 10 days). Tympanocenteses was performed at baseline; clinical response was assessed at day 12 to 16 and day 28 to 32. Two-thirds of patients were aged < 2 years. A history of recurrent, persistent, or recurrent plus persistent AOM was noted in 67, 18, and 14% of patients (86 versus 84%, respectively) and for children aged <2 years (85 versus 79%, respectively). At day 28 to 32, clinical success rates for azithromycin were superior to those for amoxicillin-clavulanate for all patients (72 versus 61%, respectively; P=0.047) and for those aged < 2 years (68 versus 51% respectively; P=0.017). Per-pathogen clinical efficacy against Streptococcus pneumoniae and Haemophilus influenzae was comparable between the two regimens. The rates of treatment-related adverse events for azithromycin and amoxicillin-clavulanate were 32 and 42%, respectively (P=0.095). Corresponding compliance rates were 99 and 93%, respectively (P=0.018). These data demonstrate the efficacy and safety of high-dose azithromycin for treating recurrent or persistent AOM.

Antimicrobial Agents and Chemotherapy, 2003, p 2663-65.

Efficacy of Single-Dose Azithromycin in Treatment of Acute Otitis Media in Children after a Baseline Tympanocentesis.

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Pfizer Global Research & Development, New London Connecticut[1] Maya Family Medicxal Center, Chicago, Illinois [2]; Hospital Nacional de Niños and Neeman-ICIC, San José, Costa Rica[3]; Hospital Infantil Juan Pablo II, Guatemal City, Guatemala[4]; Children´s Hospital of Orange County; Orange[5], Pediatrics Plus, Clovis[6], and Children´s Hospital and Health Center, San Diego[14]. California; Scottsdale Pediatric Center, Scottsdale, Arizona6; Primary Physicians Research[8] and Center for Genomic Sciences, Allegheny Singer Research Institute and Departmen of Microbiology and Immunology, MCP Hahnemann School of Medicine[18], Pittsburgh, Pennsylvania; Vienna Pediatric Associates, Vienna, Virginia [9]; Clinical Research Group, University of Chile School of Medicine[10], Centro M{edico OTOMED[11], Hospital Clínico Universidad de Chile[12], and Hospital Luis Calvo Mackenna[16], Santiago, Chile; Hill Top Research Inc., Salt Lake City Utah; University of North Texas Health Science Center at Ft. Worth, Department of Pediatric, Ft. Worth, Texas[15]; Rainbow Babies and Children´s Hospital, Cleveland, Ohio[17], and Pfizer, Inc., New York, New York[19].
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Children with acute otitis media underwent tympanocentesis and were given a single dose of 30 mg of azithromycin/kg of body weight. At day 28, the overall clinical cure rate was 206 of 242 (85%). Clinical cure rates for patients infected with Streptococcus pneumoniae (67 of 76; 88%) and Haemophilus influenzae (28 of 44; 64%) were consistent with historical rates for the 5-day dosing regimen.

Psiquiatría

XI Congreso Panamericano de Neurología, Santiago, 3-5 Octubre.

Perfil psicológico de estudiantes de medicina

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Objetivos: Describir los rasgos de personalidad en estudiantes de medicina y comparar el perfil promedio de esta muestra con el rasgo esperado para la población general.
Metodología: Se aplicó el test de personalidad 16-PF a 62 estudiantes de pregrado de la carrera de Medicina en la Universidad de Chile cursando su quinto año. Esta escala mide 16 rasgos de personalidad y 5 dimensiones globales. Los perfiles obtenidos se compararon según los esperados para la población general.
Resultados: El promedio de edad fue de 23.41 años, el porcentaje de mujeres fue fue de 46%, el de hombres 54%.
Con respecto a los promedios de la muestra en cada rasgo de personalidad, se observaron valores fuera de rango de la población general solo en 1 de ellos. En el rasgo razonamiento se encontró un promedio de 8, en rasgos de sensibilidad tensión y autosuficiencia; fue de 7 (polo alto). El resto de los promedios de rasgos se ubican dentro de los límites esperados para la población general.
Conclusiones: Los estudiantes de medicina de muestra tienden a presentar mayor pensamiento abstracto que la población general y tienden a ser sensibles, tensos, impacientes, autosuficientes, individualistas y solitarios. En el polo bajo de puntajes aparecen las variables perfeccionismo, poca atención a las normas, y poca animación.

Lancet 2003; 361: 995-1000

Treating depression in primary care in low-income women in Santiago, Chile: a randomised controlled trial.

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Background: Depression in women is one of the commonest problems encountered in primary care. We aimed to compare the effectiveness of a stepped-care programme with usual care in primary-care management of depression in low-income women in Santiago, Chile.
Methods: In a randomized controlled trial, in three primary-care clinics in Chile, 240 adult female primary-care patients with major depression were allocated stepped care or usual care. Stepped care was a 3-month, multicomponent intervention led by a non-medical health worker, which included a psycho-educational group intervention, structured and systematic follow-up, and drug treatment for patients with severe depression. Data were analyzed on an intention-to-treat basis. The primary outcome measure was the Hamilton depression rating scale (HDRS) administered at baseline and at 3 and 6 months after randomization.
Findings: About 90% of randomized patients completed outcome assessments. There was a substation between-group difference in all outcome measures in favour of the stepped-care programme. The adjusted difference in mean HDRS score between the groups was –8.89 (95% CI- 11.15 to –6.76; p<0.0001). At 6-monts' follow-up, 70% (60-79) of the stepped-care compared with 30% (21-40) of the usual-care group had recovered (HDRS score <8).
Interpretation: Despite few resources and marked deprivation, women with major depression responded well to a structured, stepped-care treatment programme, which is being introduced across Chile. Socially disadvantaged patients might gain the most from systematic improvements in treatment of depression.

J Epidemiolol Community Health 2003; 57: 501-5

Education and income: Which is more important for mental health?

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Study Objective: To assess which indicators of socioeconomic status are associated with an increases prevalence of common mental disorders. Design: Cross sectional household survey. Setting: Santiago, Chile. Participants: Random sample of adults aged 16-65 residing in private households. Main results: Less education (odds ratio 2.44, 1.70 to 2.70), and poor housing (odds ratio 1.53, 1.05 to 2.23), were the only socioeconomic status variables that remained significantly associated with an increased prevalence of common mental disorders after adjustments. The prevalence of common mental disorders was also higher among people with manual unskilled occupations, overcrowded housing, and lower per capita income but these associations disappeared after adjustment for other explanatory and confounding variables. Conclusions: There is a strong, inverse, and independent association between education and common mental disorders. However, income was not associated with the prevalence of common mental disorders, after adjusting for other socioeconomic variables. Similar results have been found in other Latin American studies but British studies tend to find the opposite, that income but not education is associated with common mental disorders. Understanding the impact of socioeconomic factors on mental health requires research in poor as well as rich countries.

American Psychiatric Association–2003 Annual Meeting, 16-23 Mayo, San Francisco, California.

Depression among low income women in primary care Santiago, Chile

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At the conclusion of this session, the participant should be able to learn more effective ways of treating depression among women in primary care clinics from deprived neighborhoods.

Objective: To compare the effectiveness of a multicomponent, stepped-care program with usual care for the tratment of depression in primary care.
Method: Randomized controlled trial. 240 female primary care patients aged 15-70 who met DSM-IV major depression criteria were randomly allocated to either usual care or the "stepped-program". Non-medical health workers led this programme the involved a psycho-educational group intervention, a structured and systematic follow-up, and pharmacotherapy. The main outcome measure was the Hamilton Rating Scale for Depression. All patients completed blinded assessments at three and six months after randomization.
Results: 90% of randomized subjects completed outcome assessments. There was a large and higgly significant difference in all outcome measures between treatment groups, in favor of the stepped-care program. The adjusted difference in mean HDRS between the two group was 9.0, 95% CI 6.8, 11.2, $p<0.001$. At six-months (CI 60,79) of the intervention group compared with 30% (CI 21,40) of the usual care had recovered (HDRS score<8).
Conclusions: In spite of the lack of resources and marked socio-economic deprivation, depressed women responded well to our treatment programme, wich is now being introduced nation wide.

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Comorbididy in Tobacco Use

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Objective: To study tobacco use in relation with psychiatric morbidity an illegal drug use among adults in Santiago.
Method: A cross-sectional study through a household survery with a probalistic sampling design was done (N=3,237,286). To determine psychiatric morbity CIS-R was used and structured questionnaire applied. Results: Sample= 3,870.52.2% were women, 47,8% were men, median age was 34 years. Income per cápita was US$120.13.3% of smokers used marijuana (men=19.2%, women=6.4%), 2.5 used cocaine (men=3.5%, womwn=1.4%), and 1.9% used paste (men=2.4%, women=1.2%). Smokers were 5.9 times (95% CI = 5.83 – 5.96) likelier to use marijuana, 5.7 (95% CI=5.56-5.85) times likelier to use cocaine, and 4,9 (95% CI=4.74-5.01) times likelier to use paste. Among people that met the criteria for psychiatric disorder, 47.1% smoked, the women with a psychiatric disorder, the risk of smoking was 1.39 (95% CI=1.39 – 1.40; p=0.00) and for men it was 1.28 (95% CI=1.27 – 1.28; p= 0.00) compared to women and men without a psychiatric disorder, respectively.
Conclusions: There is a positive association between smoking and psychiatric disorders. This study was funded by FONDECYT 1961075 and the European Comminity.

Cultural issues among Hispanics: A portrait of heterogeneity

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Summary: In recent years, several medical studies have tried to compared epidemiological, clinical, or treatment-related factors between different populations in the America continent, assuming the existence of well defined ethnic groups. Most of the Spanish-speaking immigrants living in the U.S. have been identified for these purposes as Hispanics even though they show a wide and diverse spectrum of inclusion criteria in each study. Many authors have assumed that this "Hispanic" population may constitute a homogeneous ethnic group, and that it could also be considered identical to the population from Latin America. These assumptions seem to show a lack of objective support and scientific rigor. Many epidemiological studies have shown considerable differences among the so-called "US Spanish population" even in parameters considered "hard" such as adult and child mortality, educational level, violence, fertility levels, activity, etc, suggesting a wide intra-group cultural diversity. These distinctions are even more significant when comparing cultural features among Latin American subpopulations. In psychiatric research, a clear definition of homogeneous groups and the consideration of inter-group cultural differences (i.e., Spanish-speaking Americans and Latin Americans) is extremely relevent for methodological and clinico-therapeut reasons. A recognition of potential biases when using the same methods and instruments in different contexts is needs. Some suggestions are presented to improved this important aspect of ethnicity research.

Personality and hispanic patients

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Summary: The classification of personality has generated innumerable controversies all along the history by psychiatry. In Chapter V of the revision of the ICD-10by the WHO, many terms that were usually of common usage by psychiatrists disappeared. A similar process has happened along the history of the DSM. If both classifications want to represent multicultural populations, a disadvantage in the subcategorization of the personality axis seems to have happened. Although the ICD-10 seems to be more efficient in classifying certain personality trait, many aspects that involve cultural behavior might fall equivocally as personality trait, therefore being analyzed as pathological. The development of new clinical studies will be shown in this presentation in order to clarify doubts and suggest the necessary modifications to create

clearer limits in this difficult area of diagnosis in our field, particulary when it comes to Hispanic populations.

The promise of science and its delivery in the Americas

Heerlein A, Silva C, Marchant N.

Summary: The existence and quality of human resources destined to psychiatric research have developed the field into a privileged area in the field of medicine. Most of the energy goes into the biological area of interest. Financial resources south of the Rio Grande are limited. Therefore, developing countries produce little scientific literature in mental health. Thanks to the internet most mental health workers now have access to up-to-date scientific literature. Still, many other resources such as imaging are only available to 1% of the population. The purpose of this paper is to underline how the population in the Americas has profited from research and what remains to be done four our field to be a fairer one.

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Antidepressant treatment in patients with schizophrenia

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Objective: Schizophrenia patients are often treated with antipsychotics and antidepressants. This study analysed the antidepressant prescriptions in schizophrenia.

Method: A sample 400 schizophrenic patients according to DSM-III-R criteria was ascertained. Information about drug prescriptions, age at ouset, course of symptoms and mood symptom, was obtained, Student's test was used in the analysis of the data, with a level of significance of $p=0.05$. SAS was used for all statistical analysis.

Results: Eighty-two schizophrenic patients (20.5%) received antidepressant (males: 69.5%; females: 30.5%). Antidepressants were always prescribed in combination with antipsychotics. In comparison with the total sample, the age at onset (16.5 years, DS 9.15) was significantly earlier ($p<0.05$. Sixty-eight patients (83%) reported depressive symptomatology and 33 cases (40%) showed a high risk of self-harm (suicide attempts). A tendency to chronic course was observed in sixty-two patients (76%).

Conclusions: In this sample, males patients received more antidepressant prescriptions than females. Important depressive symptomatology was also observed. Both the course of illness and the early age at onset suggest that these patients present a poor prognosis schizophrenia.

Effect of age at onset of schizophrenia on familial psychiatric morbidity.

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Objective: It has been suggested that age of anset of schizophrenia is related to the risk of familial psychiatric morbidity. The objective of this study was to examine the possible association between age at onset of illness and familial risk.

Method: Four hundred patients with DSM-III-R schizophrenia were studied. Age of onset of schizophrenia (first psychotic symptoms) and psychiatric morbidity in relatives of schizophrenic patients were determined. Chi-square test was applied for the statistical analysis of the data.

Results: The earliest onset schizophrenic patients showed the highest familial aggregation of psychiatric disorders; however, no significant differences were found ($p<0.05$), either in the total sample or in the analysis by sex.

Conclusions: The results of this study were not conclusive and did not support an association between familial risk and age of onset of schizophrenia.

Familial aggregation of affective disorders in Schizophrenic Probands.

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Objective: It has been suggested that there is a familial relationship between schizophrenia and mood disorders. The objective of this study was to compare the risk for affective disorders in the first degree relatives of schizophrenia probands (FDRS) and in the general population (GP) of Santiago, Chile.
Methods: Forty-four schizophrenic probands, according to the DSM-III-R criteria, were selected. The FDRS (n=235) were interviewed using the Composite International Diagnostic Interview (CIDI) and the DSM-III-R Chek list. Test for proportions was used in the analysis of the data; with a level of significance of p=0.05. SAS was used for all statistical analysis.
Results: Psychiatric morbidity was observed in 51.9% of FDRS and in 33.7% of GP. The difference was statistically significant (p>0.05). The morbidity risk for affective disorders in FDRS (31.5%) was significantly higher than in (19.8%) (p>0.05), both in males and females.
Conclusions: An increased familial risk for affective disorders was found in the FDRS. The results support relationship between schizophrenia and mood disorders.

Influence of age of onset on the course of schizophrenia.

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Department of Psychiatry, University of Chile.

Objective: It has been reported that age of onset of schizophrenia is one of the factors that determines the prognosis of illness. The objective of this study was to analyze the relationship between age at onset of schizophrenia and this course.
Method: A sample of 400 patients with DSM-III-R schizophrenia was ascertained. Information about age of onset (first psychotic symptoms), couse of symptoms, schizophrenic subtype according to Crow´s classification, and the number of hospitalizations was obtained. Chi-square test was used in the statistical analysis of the data. Results: The earliest onset schizophrenic patients had the highest number of rehospitalizations. They also showed a tendency of having a chronic course and were classified as mixed Crow´s subtype; however, no statistical significant differences were found (p<0.05), either in the total sample or the in the analysis by sex. Conclusions: The results of this study showed no significant associations between age at onset and course of schizophrenia.

XI Congreso Panamericano de Neurología, Psiquiatría y Neurocirugía. Santiago 3-5 Octubre 2003.

Capital social en el gran Santiago

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Objetivo: Describir variables de capital social del gran Santiago. Metodología: Entrevista estructurada a dirigentes vecinales de 196 sectores geográficos del gran Santiago. Resultados: En un 83,2% de los sectores, las personas tienen un sentido de pertenencia con el lugar, en un 75,5% confían en sus vecinos, en un 82,6% están contentos de vivir allí, en un 72,2% se prestan ayuda mutua, en un 80,1% mantienen limpio el lugar donde viven, en un 78,4% lo mantienen bonito, en un 62,1% se sienten seguras durante el día y en un 38,0% durante la noche.

En un 48,5% de los sectores de los vecinos piensan que hay delincuencia en grado importante y un 68,8% venta de drogas.
En un 88,8% y 74,9% de los sectores, las personas tienen buen acceso a servicios.
En un 63,6% de los sectores es probable que los vecinos intervengan si ven personas botando basura, en un 61,7% si ven niños insultando a una persona mayor y en un 55,7% si ven personas peleando, en un 43% cooperarían para evitar el cierre del consultorio, en un 56,8% para mejorar la sede social, en un 67,0% para arreglar la plaza y en un 87,8% para cooperar en campaña de ayuda a un vecino.
Conclusiones: Se perciben niveles de capital social comunitario relativamente altos, pero coexisten con importantes porcentajes de inseguridad ciudadana.

Síndrome premenstrual (SPM) y Trastorno Disfórico.

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Objetivo: Determinar la prevalencia de SPM y TDP en el país, describir la frecuencia de diversos síntomas y las asociaciones más relevantes Método: 305 estudiantes de la Universidad de Los Andes contestaron un cuestionario para recoger datos sociodemográficos y clínicos, y la Escala para Evaluación de Síntomas Premenstruales. Para el diagnóstico de TDP se exigió cumplir los criterios A, B, y C del DSM-IV. Para el diagnóstico de SPM sólo se requirió el criterio A. Resultados: Se encontró una prevalencia de SPM de 19% y de TDP de 11,2%. Aunque casi todas las estudiantes (99,2% tenían al menos un síntoma durante el premenstruo, el 69,8% de la muestra no presentó patología premenstrual. Todos los síntomas estudiados fueron más frecuentes en las mujeres con TDP que en las con SPM. A su vez, todos los síntomas, salvo la distensión abdominal, fueron más comunes en las mujeres con SPM que en aquellas sin patología premenstrual. Los síntomas más frecuentes en las mujeres con TDP fueron con tristeza y/o decaimiento (100%), distensión o dolor mamario (97,1%), distensión abdominal (97,1%), cambio de ánimo bruscos (94,1%), aumento de peso (94,1%), avidez específica por ciertos alimentos (91,2%) e irritabilidad (91,2%). En comparación a las mujeres sin patología premenstrual, las con TDP tenían 2,7 veces más riesgo de fumar, 3,2 más veces antecedentes depresivos, 2,6 veces más riesgo de referir estrés y 4,1 más veces posibilidades

Reumatología

Rheumatology (Oxford). 2003 Feb;42(2):308-13.

The -308 polymorphism in the tumour necrosis factor (TNF) gene promoter region and ex vivo lipopolysaccharide-induced TNF expression and cytotoxic activity in Chilean patients with rheumatoid arthritis.

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Objective: To investigate the association of the -308 polymorphism in the promoter region of the tumour necrosis factor (TNF) gene with susceptibility to the development of RA. We also explored the expression and cytotoxicity of TNF in relation to the -308 polymorphism. Methods: We recruited 92 RA patients and 42 healthy control subjects. Genotyping for the TNF promoter was performed by polymerase chain reaction-restriction fragment length polymorphism analysis. To study the overexpression of TNF we used a whole-blood culture system. TNF cytotoxicity was assessed in the L929 cell line. Results: The TNF2 allele was found in 23% of RA patients and 10% of controls. Although both groups showed high variability in serum TNF concentration, in the lipopolysaccharide-induced TNF level and in the cytotoxicity of the cytokine in the L929 cell line, these differences were not associated with the -308 TNF polymorphism. Conclusion: No associations were found between the -308 TNF promoter polymorphism, serum and ex vivo TNF levels and the cytotoxic activity of TNF in RA patients.

European League Against Rheumatism 2003.

High levels of deglycosilated anti-lipoteichoic acid-IGG, and IL-8 production in behcet´s disease.

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Background: Streptococcus sanguis has been suggest as a causative agent in Behcet´s disease (BD). Lipoteichoic acid (LTA) is a molecule associated with the cell membrane of Gram- positive bacteria. We have previously reported that LTA injected into the footpad of female lewis rats induces an anterior uveitis. These results led to the hypothesis that antigens from microorganisms may trigger autimmune reponses in-patients with BD. However there are no stidies focused in the molecular characteristics and pathogenicity of the anti-LTA antibodics. In the present study we assess the humoral and cellular immune response against LTA in a group of patients with BD and compare it to a group of patients with chronic bening oral ulcer (OU), and to normal controls.

Objectives: To assess the humoral and cellular inmune response against Lipoteichoic acid (LTA) and lipopolysaccharide (LPS), in-patients with Bechcet´s disease (BD), and compare this response with that of a group of patients with chronic bening oral ulcers (OU), and to normal controls.

Anti-LTA, anti-LPS antibodics levels and the capacity of inmmune complexes anti-LTA IgG-LTA to activate complement were studied. Exposed mannose residues in anti-LTA IgG were analyzed in the four groups. The interleukin-8 (IL-8) production by peripheral blood mononuclear cell cultures after LTA and LPS stimulation was also studied in all groups.

Results: The mannan binding protein capacity of the anti-LTA IgG antibodies was significantly higher in BD an OU groups versus normal controls. Only OU group presented higher anti-LPS IgG antibodies levels when compared to normal controls ($p<0.023$).

Clinically active BD patients showed a significantly higher IL-8 production in PBMN than other groups anly after LTA, but not after LPS, stimulation ($p<0.001$).

Conclusion: BD showed a more selective response to LTA than OU patients. Our data suggest that LTA may be an important antigen in self-perpetuation of local damage in-patients with OU and BD.

Urología

Arch Androl 2003; 49: 95-105.

Glutathione-related enzymes in cell cultures from different regions of human epididymis.

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Protection of maturing sperm from potential endogenous or exogenous harmful substances during their transit throughout the epididymis is a critical event. The authors studied the activity of gamma-glutamyl transpeptidase (GGT) and glutathione S-transferase (GST), and glutathione (GSH) levels in epithelial cell cultures from human caput, corpus, and cauda epididymides. Tissue was obtained from patients undergoing therapeutic orchidectomy for prostatic cancer. Enzymatic activity was measured in conditioned media and cellular fractions. Androgen influence was also evaluated. Both enzymatic activities were found in cellular homogenates and conditioned media from cultures of all epididymal regions. GGT activity was highest in cultures from cauda epididymis, both in conditioned media and cell fractions, while GST activity did not show regional differences in conditioned media, but exhibited higher activity in cell homogenates from cauda cultures than those obtained from corpus and caput epididymis. GSH level showed no regional difference in cell homogenates and it could not be detected in conditioned media by the method used. Presence of different concentrations of dihydrotestosterone (DHT) had no influence neither on the enzymatic activities nor GSH concentration. The results indicate that GGT and GST

are present along the human epididymis and a fraction or isoform of these enzymes might be secreted to the luminal fluid to play a detoxificative role in sperm maturation.

Prostate 2003; 57: 111-7.

Positive correlation between single or combined genotypes of CYP1A1 and GSTM1 in relation to prostate cancer in Chilean people.

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Background: The prostate cancer is a slowly progressing disease that begins decades prior to diagnosis. It has been suggested that there might be differences in susceptibility due to genetic polymorphisms in biotransformation enzyme genes. In the present work, associations between CYP1A1(Msp1), GSTM1(-/-) polymorphisms, and prostate cancer were analyzed in a case-control study. METHODS: Genomic DNA was isolated from peripheral blood samples, collected on EDTA. PCR-RFLP was used to determine simultaneously Msp1 and GSTM1(-/-) polymorphisms. Results: In cancer patients, frequency of m2 variant allele (0.377) and GSTM1(-/-) (0.362) showed statistically significant increases compared to the control group (0.262 and 0.227, respectively). The estimate relative risks (OR) were higher for individuals carrying combined CYP1A1 and GSTM1 rare genotypes, in relation to individuals carrying CYP1A1 or GSTM1 alone. Multivariate logistic regression analysis including confounding factors (age, digital examination, and PSA antigen) showed even higher risk for individuals carrying m2m2 genotype (OR = 3.99; 95% CI, 1.27-12.54), GST(-/-) genotype (OR = 2.75; 95% CI, 1.31-5.79), and m2m2/GST(-) genotype (OR = 16.63; 95% CI, 1.67-165.48). CONCLUSIONS: Taken together, these findings suggest that Chilean people carrying single or combined GSTM1 and CYP1A1 polymorphisms are more susceptible to prostate cancer. Copyright 2003 Wiley-Liss, Inc.

Urology 2003; 62: 900-4.

Gadolinium-enhanced MRI in the evaluation of minimally invasive treatments of the prostate: correlation with histopathologic findings.

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Objectives: To explore the use of magnetic resonance imaging (MRI) with gadolinium enhancement as a noninvasive method to image the extent of ablation after minimally invasive treatment. Minimally invasive methods for ablating prostatic tissue have emerged as a viable option in the treatment of prostate disease. As these devices enter the mainstream of patient care, imaging methods that verify the exact location, extent, and pattern of the ablation are needed. Methods: Nineteen patients with prostate cancer were evaluated. All received some type of minimally invasive treatment, post-treatment gadolinium-enhanced MRI sequences, and radical retropubic prostatectomy for histopathologic evaluation. Visual comparisons of gadolinium defects and areas of coagulation necrosis as seen on histopathologic evaluation were made by us. Volumetric and two-dimensional area measurements of the ablation lesions were also compared for correlation between the MRI and histopathologic results. Result: Gadolinium-enhanced MRI could be matched to histopathologic findings by visual comparison in 17 of the 19 cases. Surgically distorted histopathologic specimens and a small periurethral lesion caused 2 patients to have MRI and histopathologic results that could not be matched. Complete volumetric measurements were available for 16 of the 19 patients and correlated strongly (r = 0.924). The two-dimensional area data for all patients also showed significant correlation (r = 0.886). Conclusions: Correlation with histopathologic findings showed gadolinium-enhanced MRI to be useful for determining the location, pattern, and extent of necrosis caused within the prostate by minimally invasive techniques. Gadolinium-enhanced MRI gives the urologist a useful tool to evaluate the effectiveness of new minimally invasive therapies.

U.P.C.

Free Radic Biol Med 2003 Aug 1; 35: 257-65.

Thyroid hormone-induced oxidative stress triggers nuclear factor-kappaB activation and cytokine gene expression in rat liver.

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Nuclear factor-kappaB (NF-kappaB) is a redox-sensitive factor responsible for the transcriptional activation of cytokine-encoding genes. In this study, we show that 3,3,5-triiodothyronine (T(3)) administration to rats activates hepatic NF-kappaB, as assessed by electrophoretic mobility shift assay. This response coincides with the onset of calorigenesis and enhancement in hepatic respiration, and is suppressed by the antioxidants alpha-tocopherol and N-acetylcysteine or by the Kupffer cell inactivator gadolinium chloride. Livers from hyperthyroid rats with enhanced NF-kappaB DNA-binding activity show induced mRNA expression of the NF-kappaB-responsive genes for tumor necrosis factor-alpha (TNF-alpha) and interleukin- (IL-) 10, as evidenced by reverse transcription-polymerase chain reaction assay, which is correlated with increases in the serum levels of the cytokines. T(3) also increased the hepatic levels of mRNA for IL-1alpha and those of IL-1alpha in serum, with a time profile closely related to that of TNF-alpha. It is concluded that T(3)-induced oxidative stress enhances the DNA-binding activity of NF-kappaB and the NF-kappaB-dependent expression of TNF-alpha and IL-10 genes.