

**Complete anterior capsule contraction after phacoemulsification with acrylic intraocular lens and endocapsular ring implantation**

**Javier Moreno-Montañés, MD, PhD, Hortensia Sánchez-Tocino, MD, Rosa Rodríguez-Conde, MD**

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A 69-year-old man with pseudoexfoliation syndrome and bilateral cataract had phacoemulsification with continuous curvilinear capsulorhexis and implantation of a Morcher endocapsular ring and AcrySof® acrylic intraocular lens (IOL) (Alcon). Two months later, the patient had vision loss in the left eye with a visual acuity of 20/500. He presented anterior capsule fibrosis in both eyes, complete occlusion of the capsule opening in the left eye and mild occlusion in the right eye. After a neodymium:YAG laser anterior capsulotomy in the left eye, visual acuity was 20/20. This case shows that endocapsular ring implantation does not prevent anterior capsule contraction syndrome but can prevent IOL decentration.

**Extensive corneal epithelial defect associated with internal hordeolum after uneventful laser in situ keratomileusis**

**Miguel J. Maldonado, MD, PhD, José R. Juberías, MD, PhD, Javier Moreno-Montañés, MD, PhD**

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This report illustrates a retrospective case review in which extensive corneal epithelial ulceration occurred concomitantly with an internal hordeolum in the inferior forniceal conjunctiva 24 hours after an uneventful laser in situ keratomileusis. The internal hordeolum and epithelial defect were successfully managed using a bandage soft contact lens, a course of topical dexamethasone and tobramycin, and generous lubrication.

**Retinal Thickness Study with Optical Coherence Tomography in Patients with Diabetes**

**Hortensia Sánchez-Tocino, Aurora Álvarez-Vidal, Miguel J. Maldonado, Javier Moreno-Montañés and Alfredo García-Layana**

*From the Department of Ophthalmology, University Clinic of Navarra, Pamplona, Navarra, Spain*

*Abstract of: Investigative Ophthalmology and Visual Science. 2002;43:1588-1594*

**Purpose:** To quantitatively assess retinal thickness by optical coherence tomography (OCT) in normal subjects and patients with diabetes. This study was intended to determine which retinal thickness value measured with OCT best discriminates between diabetic eyes, with and without macular edema.

**Methods:** OCT retinal thickness was measured by a manual technique in a total of 26 healthy volunteers (44 control eyes) and 85 patients with diabetes (148 eyes) with the clinical diagnosis of no diabetic retinopathy (45 eyes), nonproliferative diabetic retinopathy without clinically significant macular edema (CSME; 54 eyes), proliferative diabetic retinopathy without CSME (21 eyes), and 28 eyes with diabetic retinopathy with CSME. Independent predictors of the presence of CSME were quantified by using univariate and multivariate logistic regression analyses. Receiver operating characteristic (ROC) curves were generated to evaluate and compare the predictor variables. The correlation of retinal thickness measurements and visual acuity was calculated.

**Results:** There were statistically significant differences in foveal thickness between control eyes and all the other eye groups ( $P = 0.001$ ). Diabetic eyes with CSME had a statistically significant greater thickness in each of the areas compared with the other groups. In a multivariate logistic regression model, foveal thickness was a strong and independent predictor of CSME (odds ratio [OR], 1.037; 95% confidence interval [CI] 1.02—1.05). The area under the ROC curve of this predictor variable was 0.94 ( $P = 0.001$ ). For a cutoff point of 180  $\mu\text{m}$ , the sensitivity was 93%, and specificity was 75%. Foveal thickness correlated with visual acuity in a log minimum angle of resolution (logMAR) scale (Spearman's  $\rho = 0.9$ ,  $P = 0.001$ ).

**Conclusions:** These results suggest that foveal thickening over 180  $\mu\text{m}$  measured by OCT may be useful for the early detection of macular thickening and may be an indicator for a closer follow-up of the patient with diabetes.

**Comparison of unidimensional and bidimensional measurements in metastatic non-small cell lung cancer**

**Cortes J, Rodríguez J, Díaz-González JA, Garzón C, Gurrpide A, Arbea L, Gil-Bazo 1, Navarro V, Cambeiro M, Nicolás AI, Martín-Algarra S, García-Foncillas J, Calvo E.**

*Department of Oncology, Clínica Universitaria de Navarra, Avenida de Pio XII. 36, 31008 Pamplona, Spain. jccastan@unav.es*

*Abstract of: Br J Cancer 2002 Jul 15;87(2):158-60*

Tumour response evaluation after chemotherapy has become crucial in the development of many drugs. In contrast

to the standard bidimensional WHO criteria, the recently described Response Evaluation Criteria In Solid Tumors are based on unidimensional measurements. The aim of the present study was to compare both methods in patients with metastatic non-small cell lung cancer. One hundred and sixty-four patients treated with two cisplatin-paclitaxel-based chemotherapy schedules between June 1994 and December 2000 were analysed. The measurements were reviewed by an independent panel of radiologists. Patient characteristics were: median age of 55 years (range 24-77 years) and a male to female ratio of 129: 35. Adenocarcinoma and squamous carcinoma were the most common histologies. Vinorelbine was the third drug used in 77 patients and gemcitabine in 87. The ratio unidimensional/bidimensional was as follows: response 85 : 85; stable disease 32 : 32; progression 47: 42 and not assessable 0 : 5. Kappa for agreement between responders was 0.951 (95% CI: 0.795-1.0) (P<0.001). Both WHO criteria and Response Evaluation Criteria In Solid Tumors give similar results in assessing tumour response in patients with non-small cell lung cancer after chemotherapy. The unidimensional measurement could replace the more complex bidimensional one.

### Combined Irinotecan, Oxaliplatin and 5-Fluorouracil in Patients with Advanced Colorectal Cancer. A feasibility pilot study

Calvo E, Cortes J, González-Cao M, Rodríguez J, Aramendia JM, Fernández-Hidalgo O, Martín-Algarra S, Salgado JE, Martínez-Monge R, De Irala J, Brugarolas A.

Department of Oncology, Division of Medical Oncology, Clínica Universitaria de Navarra, University of Navarra, Navarra, Spain

Abstract of: *Oncology* 2002;63(3):254-65

**Objectives:** To evaluate the feasibility and a possible activity range of combination irinotecan (CPT-11), oxaliplatin, and 5-FU in advanced colorectal cancer (ACC).

**Patients and Methods:** A total of 53 patients (51% chemoresistant) were treated. Twenty-eight received monthly intravenous oxaliplatin (120 mg/m<sup>2</sup>) and CPT-11 (250 mg/m<sup>2</sup>) on day 1 and a course of 5-FU; these constituted the IRI250 group. Twenty-five received monthly intravenous oxaliplatin (120 mg/m<sup>2</sup>), CPT-11 (300 mg/m<sup>2</sup>) on day 1, and a course of 5-FU (IRI300 group). 5-FU administration was carried out as follows. Those with predominant hepatic disease (n = 32) received an intra arterial infusion of 5-FU (2,500 mg/day on days 1-4); these were the IA-FU group. The remaining 21 patients received intravenous 5-FU (2,600 mg/m<sup>2</sup>) plus leucovorin 500 mg/m<sup>2</sup> on days 1 and 15); these constituted the IV-FUFOL group.

**Results:** Intention-to-treat response rate was 54.7% (4 CR, 7.5%). Twelve patients (22.5%) had stable disease; only 4

(7.5%) progressed. Median progression-free and overall survivals were 10 and 18 months, respectively. One-year progression-free and overall survival rates were 44.3 and 67.4%, respectively. Grade 3-4 toxicities included diarrhea (45.3% of patients), neutropenia (52.8%), mucositis (13.2%), and emesis (11.3%). There were 3 treatment-related deaths (5.7%), all in the IA-FU/IRI300 subgroup. Severe adverse effects requiring chemotherapy dose adjustment were observed in 67.9% of the patients, with odds ratios 9.04-fold higher in the IA-FU/IRI300 group (95% CI: 1.07-76.20) and 0.23-fold lower in the IV-FUFOL/IRI250 group (95% CI: 0.05-0.97).

**Conclusion:** This combination seems to have substantial activity in ACC. Overall toxicity was unacceptable in the IA-FU and IRI300 groups, with diarrhea and cytopenia constituting the dose-limiting side effects.

### Effect of ursodeoxycholic acid on methionine adenosyltransferase activity and hepatic glutathione metabolism in rats

CM Rodríguez-Ortigosa, RN Cincu, S Sanz, F Ruiz, J Quiroga, J Prieto

Abstract of: *Gut* 2002;50:701-706

**Background and aims:** Both bile salts and glutathione participate in the generation of canalicular bile flow. In this work, we have investigated the effect of different bile salts on hepatic glutathione metabolism.

**Methods:** Using the isolated and perfused rat liver, we studied hepatic glutathione content, and metabolism and catabolism of this compound in livers perfused with taurocholate, ursodeoxycholate, or deoxycholate.

**Results:** We found that in livers perfused with ursodeoxycholate, levels of glutathione and the activity of methionine adenosyltransferase (an enzyme involved in glutathione biosynthesis) were significantly higher than in livers perfused with other bile salts. In ursodeoxycholate perfused livers, methionine adenosyltransferase showed a predominant tetrameric conformation which is the isoform with highest activity at physiological concentrations of substrate. In contrast, the dimeric form prevailed in livers perfused with taurocholate or deoxycholate. The hepatic activities of  $\gamma$ -glutamylcysteine synthetase and  $\gamma$ -glutamyltranspeptidase, enzymes involved, respectively, in biosynthetic and catabolic pathways of glutathione, were not modified by bile salts.

**Conclusions:** Ursodeoxycholate specifically enhanced methionine adenosyltransferase activity and hepatic glutathione levels. As glutathione is a defensive substance against oxidative cell damage, our observations provide an additional explanation for the known hepatoprotective effects of ursodeoxycholate.

## Cutaneous polyarteritis nodosa

**A. Bauzá, A. España and M. Idoate\***

*Departments of Dermatology and \*Pathology, University Clinic of Navarra, School of Medicine, Pamplona, Spain*

*Abstract of: British Journal of Dermatology 2002; 146: 694-699*

Classic polyarteritis nodosa (PAN) is a segmentary leucocytoclastic vasculitis that affects small- and medium-sized arteries. In 1931, Lindberg (*Acta Med Scand* 1931; 76: 183-225) described the existence of a cutaneous variant of PAN, without visceral involvement and with a more favourable prognosis. We present four patients diagnosed with cutaneous PAN in our hospital between 1987 and 1998. The study group was composed of three women and one child, whose ages ranged from 11 to 70 years old. The follow-up period was between 2 and 13 years. Each patient was submitted for an initial clinical, histological and laboratory evaluation and subsequent follow-up. The presence of nodules was the most frequent cutaneous lesion, preferentially located in the lower limbs. The erythrocyte sedimentation rate was the only parameter that was altered in all patients. Cutaneous biopsies from all patients showed a segmentary leucocytoclastic vasculitis in the arteries of the deep dermis and/or hypodermis. Direct immunofluorescence was positive in just one patient. No visceral involvement was found in any patient. There is confusion about the correct definition of cutaneous PAN. Some clinical findings, such as nodules or livedo reticularis, typical of cutaneous PAN suggest a good prognosis; however, we consider that it is necessary to evaluate these patients for systemic involvement for the possibility of arteritis in other organs as the term polyarteritis suggests.

**Key words:** Classic polyarteritis nodosa. Cutaneous polyarteritis nodosa. Livedo reticularis. Nodules.

## Cutaneous umbilical endosalpingiosis with severe abdominal pain

**P Redondo†\*, M Idoate‡, C Corella§**

*Departments of †Dermatology, ‡Pathology and §Gastroenterology, University Clinic of Navarra, PO Box 192, 31080 Pamplona, Spain.*

*\*Corresponding author, tel. +34 48 255400; fax +34 48 172294; E-mail: predondo@unav.es*

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Cutaneous endosalpingiosis is a very rare entity, and to our knowledge umbilical location has been reported in only one patient who developed salpingectomy shortly after. We report cutaneous umbilical endosalpingiosis associated with severe abdominal pain that disappeared after surgical treatment.

**Key words:** Cutaneous endosalpingiosis. Endometriosis. umbilical.

## Tratamiento del carcinoma renal

**J. Arocena García-Tapia, J. López Ferrandis, D. Sánchez Zalbarido, J.M<sup>a</sup> Recojo Balboa, J.M. Fernández Montero, D. Rosell Costa, J.E. Robles García, J.J. Zudaire Bergera, J.M<sup>a</sup> Berrián Polo**  
*Departamento de Urología. Clínica Universitaria de Navarra. Pamplona*

*Abstract of: Actas Urol Esp. 26 (8):541-545, 2002*

La cirugía radical constituye el tratamiento estándar en el carcinoma renal. En los casos de tumores únicos y menor de 4 cm y en los tumores renales en pacientes monorrenos, la nefrectomía parcial está estandarizada como tratamiento de elección.

La tasa de respuesta en el carcinoma renal metastásico con las diversas modalidades de tratamiento inmunoterápico varían de un 15 a un 35%. siendo respuestas de corta duración.

**Palabras clave:** Cáncer renal. Tratamiento. Inmunoterapia

**Key words:** Renal cancer. Treatment. Immunotherapy.

## <sup>18</sup>F-fluoro-2-deoxyglucose-positron emission tomography in the evaluation of nonseminomatous germ cell tumours at relapse

**O. Sánchez, J.J. Zudaire, J.M. Fernández, J. López, J. Arocena, G. Sanz, M. Giménez\*, O. Rosell, J.E. Robles and J.M. Berrián**  
*Department of Urology and \*Nuclear Medicine, Facultad de Medicina, Clínica Universitaria, Universidad de Navarra. Pamplona, Spain*

*Abstract of: BJU International (2002);89:912-916*

**Objectives:** To compare the performance of <sup>18</sup>F-fluoro-2-deoxyglucose-positron emission tomography (FDG-PET) and computed tomography (CT) in the follow-up of nonseminomatous germ cell tumours (NSGCT) in the retroperitoneum.

**Patients and methods:** FDG-PET was used 25 times in 15 patients diagnosed with NSGCT. At the time of diagnosis five patients each were in stage I, II and III. Five patients had pure embryonal carcinoma, two had yolk sac tumours, one choriocarcinoma and seven had mixed tumours.

**Results:** Eleven patients either presented with retroperitoneal disease or this did not disappear after chemotherapy.

The results of both examinations coincided in 18 cases and were contradictory in the other seven, the difference being statistically significant ( $P = 0.042$ ).

**Conclusion:** In these patients FDG-PET detected the retroperitoneal relapse of NSGCT, in advanced stages treated with surgery plus chemotherapy, earlier than did CT; it also detected the presence of mature teratoma in residual retroperitoneal masses more accurately than CT. More extensive trials are needed before making conclusions about FDG-PET imaging as a routine method for NSGCT.

**Key words:** Nonseminomatous germ cell tumour. Positron emission tomography. Fluorodeoxyglucose. Computed tomography.

### Allergy to pine nut

**M. A. Añó, J. P. Maselli, M.<sup>a</sup> L. Sanz, and M. Fernández-Benítez**

*Departamento de Alergología e Inmunología Clínica Pamplona, Spain. Clínica Universitaria de Navarra, Universidad de Navarra,*

*Abstract of: Allergol et Immunopathol 2002;30(2):104-108*

**Background:** food allergy is highly prevalent in our environment, especially among atopic patients. *Pinus pinea* is common in our region and its fruit, the pine nut, is allergologically important. Several cases have been reported in the literature that demonstrate the existence of common antigenic bands between pine nut and almond. In this study we try to assess this finding and the possible existence of common allergens by *in vitro* techniques.

**Methods and results:** we present a 10-year-old boy, previously diagnosed of seasonal rhinoconjunctivitis with sensitisation to grass and olive pollen, who had so anaphylactic reaction after eating pine nut. We performed *in vivo* (prick test, prick-by-prick) and *in vitro* tests (total and specific IgE determinations [CAP-FEIA]), histamine release test, and immunoblotting (SDS-PAGE). We also reviewed the literature through the MEDLINE database in PubMed.

**Conclusions:** because pine nut is commonly consumed in our environment, the prevalence of allergic reactions is probably considerable and these reactions take place at so early age. We demonstrate the existence of common antigenic proteins between pine nut and peanuts.

**Key words:** Anaphylaxis. Pine nut. Immunoblotting. Cross reactivity to nuts. Food allergy.

### Respiratory Infection in Asthma

**M. Fernández-Benítez, M. Añó, J.P. Maselli, and M.L. Sanz**

*Department of Allergology and Clinical Immunology, University Clinic of Navarra, University of Navarra, School of Medicine, Pamplona, Spain*

*Abstract of: J Invest Allergol Clin Immunol 2002;Vol. 12(1):48-51*

Ever since the first decades of the 20th century, some authors have given respiratory infection triggered by bacteria an etiologic role in bronchial asthma, focusing on infection and the asthmatic response. In 1995 our group already presented a study in this sense on nasal secretion cultures and the relationship between IgE and sensitization to allergens. There is a significant association between patients with sensitization to *Dermatophagoides*, high levels of total IgE, and positive culture to *Staphylococcus aureus*. Following studies by Norn, we performed a study with 40 children, aged 2-14 years, where we observed that children with sensitization to mites and a positive culture had higher levels of histamine release than did children with negative culture and controls, the differences being significant. We also found, like other authors, that the joint presence of *Staphylococcus aureus* and *Dermatophagoides pteronyssinus* potentiates antigen-specific histamine release.

In recent years, with the increasing prevalence of bronchial asthma being studied, the role that infection could play in this increase is being considered again among other factors. As participants of the ISAAC project and using the same methods as in this study, we performed a simultaneous questionnaire with questions related with triggering and contributing factors, etc., including respiratory infection. We found an association between having had more than three episodes of "bronchitis" with fever and lasting for longer than seven days in the last year and having ever had asthma (OR 29.09). This association is still greater with having had wheezing in the last 12 months (OR 43.26), a finding that it is also associated with requiring attention in an emergency room (OR 30.65). From these results, we concluded that respiratory infection is an aggravating factor of asthma, something we already knew.

in order to have our own experience, we studied serum interleukin 4 (IL4) and interferon gamma (IFN $\gamma$ ) in a sample of 41 children aged 3 to 17 years. The most frequent values of IL-4 ranged between 0.25 and 0.40 ng, and very low dispersion was found in the sample, which did not allow correlation with other parameters. Regarding IFN $\gamma$ , we found values between < 5pg/ml and 605 pg/ml.

When we studied children under treatment with antigen-specific immunotherapy, we observed mean values of IFN $\gamma$  of 115.86 pg/ml, whereas the ones who did not follow this treatment or had followed it for less than one year had a mean of 66.06 pg/ml, these differences being significant ( $p = 0.035$ ), and proving a Th1 response to immunotherapy. This significance is not found if children who have been under immunotherapy for less than one year are included.

When we studied children with bacterial immunotherapy, we found that the mean IFN $\gamma$  value in children under immunotherapy for longer than one year was 56.4pg/ml, whereas in children with no immunotherapy it was 101.75 pg/ml ( $p = 0.034$ ). We conclude that bacterial immunotherapy modifies the Th1 response, inhibiting it in those children with greater susceptibility to infections.

**Key words:** Respiratory infection. Bronchial asthma. IL-4. IFN $\gamma$ . Immunotherapy.

**Thrombopenic purpura induced by a monoclonal antibody directed to a 35-kilodalton surface protein (p35) expressed on murine platelets and endothelial cells**

Rodríguez-Calvillo M, Gabari I, Duarte M, Mazzolini G, Rifon J, Rocha E, Prieto J, Melero I

*Department of Medicine, University of Navarra, Pamplona, Spain*

*Abstract of: Exp Hematol 2001 May;29(5):589-95*

**Objective:** With the aim of obtaining monoclonal antibodies (mAbs) against mouse endothelial surface antigens, immunization of rats with a mouse-derived endothelial cell line (PY4.1) and subsequent hybridoma production were performed.

**Materials and methods:** One of the mAbs produced by hybridoma EOL5F5 was selected for its surface binding to endothelial cell lines, and identification of the mAb-recognized antigen was performed by immunoprecipitation. Experiments were performed to analyze the effects of EOL5F5 on systemic administration to mice.

**Results:** EOL5F5-recognized antigen was a single band of 35 kDa under reducing and nonreducing conditions, features that do not match other known differentiation antigens with comparable tissue distribution. In vivo administration of purified EOL5F5 mAb to mice (n = 20) induced intense cutaneous purpura as well as severe but transient thrombocytopenia. Expression of EOL5F5-recognized antigen was detected on platelets from which it immunoprecipitated a moiety of identical electrophoretic pattern in SDS-PAGE, as the one recognized on endothelial cells. Immunohistochemically, EOL5F5-recognized antigen (p35) also was expressed on dermal capillaries, suggesting that, in addition to thrombocytopenia, damaging effects of the antibody on endothelial cells also might cause the observed purpura.

**Conclusions:** Our results show induction of thrombocytopenic purpura in mice with an mAb against a single antigenic

determinant expressed on both platelets and endothelium. EOL5F5 mAb injection sets the stage for useful experimental models that resemble immune thrombocytopenic purpura.

**Alpha(v)beta(3) integrin-mediated adenoviral transfer of interleukin-12 at the periphery of hepatic colon cancer metastases induces VCAM-1 expression and T-cell recruitment**

Mazzolini G, Narvaiza I, Bustos M, Duarte M, Tirapu I, Bilbao R, Qian C, Prieto J, Melero I  
*Gene Therapy Unit, University of Navarra School of Medicine, C/Irunlarrea, 1 31008 Pamplona, Spain.*

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We previously reported that systemic injection of recombinant adenovirus resulted in a rim of gene transduction around experimental liver tumor nodules. This zone of higher infection is dependent on the alpha(v)beta(3) integrin, acting as an adenovirus internalization receptor, which is overexpressed in tissues surrounding liver metastases. When a recombinant adenovirus encoding interleukin-12 (AdCMVIL-12) is given into a subcutaneous tumor nodule in mice also bearing concomitant liver tumors, a fraction of AdCMVIL-12 reaches the systemic circulation and infects liver tissue, especially at the malignant/healthy tissue interface. As a result of the expression at this location of the interleukin-12 transgenes, VCAM-1 is induced on vessel cells and mediates the recruitment of adoptively transferred anti-tumor cytolytic T-lymphocytes. These studies provide mechanistic explanations for the potent therapeutic synergy observed between interleukin-12 gene transfer and adoptive T-cell therapy.