

porciona el bien de todos los enfermos, quienes tienen la misma probabilidad de alcanzar beneficio; y 3) En el caso que los resultados no fueran así, se compensa de alguna forma el grupo que ha salido perdiendo.

Para hacer compatible la ética médica y la ética científica con intereses de los pacientes se pueden esgrimir los dos argumentos fundamentales: El servicio a la comunidad y el respeto al individuo.

Desde la primera, apuntando al bien común, la participación de los pacientes puede ser contemplada como una exigencia pública o social, al igual que pagar impuestos, cuidar el medio ambiente, servir al ejército o donar órganos. No sería prudente desarrollar la oportuna legislación sin un amplio debate cultural, profesional, social y político.

Desde la segunda perspectiva, la del respeto al individuo, la participación de los pacientes ha de regularse mediante contrato que defina con transparencia legal y médica el carácter experimental, la conveniencia e interés previsible sanitario o social, los resultados esperables, los riesgos y complicaciones, el posible sacrificio personal del participante y las compensaciones de diverso género que pudieran haber lugar.

Seguramente esta normativa reduciría el número de ensayos clínicos, pero los que se hicieran tendrían más calidad.

De cualquier forma para continuar y enriquecer el debate y lograr una respuesta éticamente correcta a los ensayos clínicos hay que contar con la opinión de los propios enfermos. Es probable que cuando comiencen a participar no quieran ser mártires sino científicos exigentes y responsables. La ética debe apelar a su colaboración.

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PLANTINUM WIRE EMBOLIZATION OF AN INTRAHEPATIC ARTEIOPORFAL FISTULA

■ José I. Bilbao, Jesús M. Longo; M. D., Jesús D. Aquerreta; M. D., Jaime Rodríguez-Cabello; M. D., and Amelia Fernández, M. D. Department of Radiology, University Clinic of Navarra, Pamplona, Navarra, Spain. *Amer. J. Gastroent.* (1990) 85, 8507-8509. ■ We report a case of arterioportal fistula in the right hepatic lobe. The lesion was selectively catheterized with an open-ended guidewire and successfully embolized with small pieces of platinum wire.

THE ROLE OF FIBRINOLYSIS IN PATIENTS WITH SEVERE CHRONIC LIVER DISEASE

■ J. A. Páramo, F. Fernández, B. Cuesta, J. Rifón, A. Pinacho, E. Rocha. Hematology Service. University Clinic. University of Navarra. Pamplona. Spain. *Biol. Clin. Hemat.* (1990). 12, 61-64. ■ **ABSTRACT:** The overall fibrinolytic activity and plasma concentrations of tissue-type plasminogen activator (t-PA) activity and antigen (t-PA AG), plasminogen activator inhibitor 1 (PAI-1 Ag), plasminogen and alpha 2-antiplasmin (alpha 2-AP) were studied in 66 patients with severe liver disease caused by cirrhosis (n=34) or chronic hepatitis (n=32) and compared to that of a control group (n=30) of healthy subjects. There was a significant increase of t-PA Ag and PAI-1 Ag (p<0,0001) and a marked reduction of plasminogen and alpha 2-AP (p<0,01) in patients as compared to controls. A correlation between t-PA and bilirubin was observed. Thus, the marked elevation of t-PA and the reduction of alpha 2-AP in severe liver disease clearly contributes to excessive fibrinolysis, t-PA Ag can be a marker of severe liver defects. ■ **Key words;** Fibrinolysis, liver disease, tissue-type plasminogen activator, alpha 2-antiplasmin.

THE BLINK REFLEX IN PATIENTS WITH HEPATHIC TORSION DYSTONIA

■ K. Nakashima, M. D.; J. C. Rothwell, Ph. D.; P. D. Thompson, FRACP; B. L. Day, DPhil; A. Berardelli, M. D.; R. Agostino, M. D.; J. Artieda, M. D.; S. M. Papas, M. D.; J. A. Obeso, M. D.; C. D. Marsden, F. R. S. (*Arch. Neurol.* 1990;47:413-416). ■ The blink reflex and its recovery cycle were examined in 57 patients with idiopathic dystonia affecting different parts of the body. The group comprised nine patients with generalized and 15 with segmental forms, 19 with torticollis, and 14 with focal arm dystonia. None had blepharospasm. The duration and amplitude of the R2 component of the blink reflex showed only minor changes. However, its recovery cycle to paired supraorbital nerve stimuli was abnormal in all groups of patients, except those with focal arm dystonia. These findings may be interpreted as showing abnormal control of the interneuronal networks mediating the blink reflex in patients with dystonia affecting sites other than the facial muscles. The fact that the principal changes were seen in patients with torticollis, and generalized or segmental dystonia, suggests that the extent of dystonia (rather than the severity) and, therefore, the close proximity to the cranial muscles was important in determining the extent of the abnormal interneuron function.

ANÁLISIS DE LA INFLUENCIA DE LOS CRITERIOS DE DIALISIS ADECUADA SOBRE LA MORBIMORTALIDAD DE LOS PACIENTES EN PROGRAMA DE HEMODIALISIS SEDYT, 1990, 11, 9-4

■ F. Maduell, J. Díez, R. Díaz-Tejero, N. Esparza, P. Errasti, A. Purroy

■ **RESUMEN:** Según el National Cooperative Dialysis Study existen tres criterios de diálisis adecuada: mantener un nitrógeno uréico medio en el tiempo menor o igual a 50 mg/dl; mantener la tasa de catabolismo proteico entre 0,8 y 1,4 gr/kg/día y mantener el índice a nivel de diálisis normalizado por el peso corporal entre 0,8 y 1,5. Para valorar si la observancia de tales criterios comporta una menor morbimortalidad de los pacientes en hemodiálisis, hemos analizado, durante dos períodos de tiempo de un año de duración, la presentación de complicaciones médico-quirúrgicas relacionadas con la uremia y/o hemodiálisis, las necesidades transfusionales y la velocidad de conducción nerviosa en un grupo de 25 pacientes, sin enfermedad sistémica relevante, sometidos a diálisis convencional, con membranas de cuprofano, a razón de tres sesiones semanales. Durante el primer año, las pautas individualizadas de hemodiálisis no se ajustaron a los criterios de diálisis adecuada anteriormente reseñados. Durante el segundo año el programa de diálisis de cada enfermo se estableció a partir de la valoración continuada de dichos criterios. Durante el primer período se presentaron 15 complicaciones, de las cuales 11 requirieron ingreso hospitalario. Durante el segundo período fueron cinco las complicaciones, siendo tres las tratadas en régimen de ingreso hospitalario.

Estos resultados sugieren que la observancia de los criterios de diálisis adecuada es beneficiosa para los pacientes en hemodiálisis, pues disminuyen la frecuencia y la severidad de las complicaciones que presentan.

■ **Palabras clave:** Hemodiálisis, diálisis adecuada, morbimortalidad.

GROUND-GLASS HEPATOCYTES; LIGHT AND ELECTRON MICROSCOPY. CHARACTERIZATION OF THE DIFFERENT TYPES

■ J. Jaime Vázquez. Department of Pathology, University of Navarra, Pamplona, Spain. *Hist. Histopath* (1990) 5, 379-386. ■ **SUMMARY:**

Morphological observations of paraffinembedded histological sections stained with H&E led to the discovery of some cytoplasmic changes which occur in different conditions, although they look alike under the light microscope. These hepatocytic changes consisted basically of homogeneous areas which are weakly eosinophilic in H&E-stained sections. They are frequently referred to as «inclusion» bodies, even when they are not true inclusions. The hepatocytic changes observed in HBsAg carriers, in chronic alcoholic patients treated with cyanamide to discourage them from drinking alcohol, in Lafora's disease, and in glycogenosis type IV, look very similar in paraffin sections stained with H&E. Nevertheless, they can be differentiated using ancillary techniques. On electron microscopy they do not look alike. Of particular interest are the «inclusion» bodies induced by cyanamide, a predictable and reproducible lesion, which in man eventually leads to cirrhosis. Other types of hepatocytic changes also giving a

rather vague «ground-glass» appearance to the cytoplasm are those resulting from intracytoplasmic accumulation of proteins, particularly fibrinogen, and those observed in patients treated with different drugs. ■ **Key words:** Ground-glass hepatocytes, liver-cell inclusion, HbsAg, cyanamide, Lafora's disease, glycogenosis type IV, Fibrinogen inclusions.

EFFECT OF KETOTIFEN ON THE METHYLTRANSFERASE ACTIVITY OF ASTHMATIC PATIENTS

■ J. G. Castillo, P. M. Gamboa, F. Santos and A. Oehling. Department of Allergology and Clinical Immunology. Faculty of Medicine. University of Navarra. Pamplona, Spain. ■ **SUMMARY:**

The results of this study have revealed that asthmatic individuals have less methyltransferase activity compared to healthy individuals. This is reflected in a less fluidity of the plasmatic membrane and thus, presents with less beta-receptors compared to healthy subjects. Ketotifen is capable of partially reversing this situation where it stimulates methyltransferase activity of asthmatic individuals approaching the enzyme activity to healthy individuals. ■ **Key-words:** Asthma ketotifen, methyltransferase activity.

TYPES 1 AND 2 PLASMINOGEN ACTIVATOR INHIBITOR AND TUMOR NECROSIS FACTOR ALPHA IN PATIENTS WITH SEPSIS*

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We have determined the plasma concentrations of types 1 and 2 of plasminogen activator inhibitor (PAI-1 and PAI-2), tumor necrosis factor (TNF-α) and endotoxin in 47 patients with bacterial infection (22 patients presented with blood cultures). Results were compared with those observed in 30 healthy subjects. There was a significant increase in PAI-1 and TNF-α in patients as compared to controls ($p < 0,0001$), whereas no differences for PAI-2 were observed. PAI-1 and TNF-α were significantly higher in 18 patients with gram-negative bacteremia as compared to all other patients ($p < 0,0001$), whereas no differences for PAI-2 were observed. PAI-1 and TNF-α were significantly higher in 18 patients with gram-negative bacteremia as compared to all other patients ($p < 0,0001$). However, no correlation between the analyzed parameters and either endotoxin or clinical outcome was observed. We conclude that there is an increase of PAI-1 and TNF-α in patients with sepsis, which is not related to the endotoxin concentration. Our results suggest that PAI-1, but not PAI-2, is the main plasminogen activator inhibitor in human sepsis.

DOUBLE-BLIND PLACEBO-CONTROLLED STUDY OF THE ANTIHYPERTENSIVE EFFICACY OF NITRENDIPINE IN PATIENTS SUBMITTED TO BLOOD PRESSURE AMBULATORY MONITORING

■ J. Honorato, J. Azanza, N. Guindo, and J. R. Suárez. Department of Clinical Pharmacology, Navarra university Clinic,

Pamplona, Spain. Current therapeutic research. Vol., 46, no. 4, October, 1989. ■ **ABSTRACT:** The antihypertensive effect of nitrendipine was assessed by means of blood pressure ambulatory monitoring in a double-blind, randomized, placebo-controlled study. twenty-four mild to moderate hypertensive patients were assigned either to nitrendipine treatment (20 mg. once daily) or matched placebo for six weeks. The nitrendipine group showed a significant reduction in systolic blood pressure after only two weeks ($P < 0.02$) and in diastolic blood pressure after four weeks ($P < 0.001$). Furthermore, a significant decrease in diastolic blood pressure was observed throughout 24 hours ($P < 0.001$), especially during the day, while no hypotensive effect on the normal values recorded at night was observed. This study confirms the efficacy of nitrendipine administered in a dose of 20 mg. once daily in mild to moderate hypertensive patients.

CELL LOSS AND NUCLEAR HYPERTROPHY IN TOPOGRAPHICAL SUBDIVISION OF THE NUCLEUS BASALIS OF MEYNERT IN ALZHEIMER'S DISEASE

■ I. Iraizoz; S. de Lacalle, and L. M. Gonzalo. Department of Anatomy, Faculty of Medicine, University of Navarra, 31080 Pamplona, Spain. Neuroscience. Vol. 41, n. 1, pp. 33-44, 1991. ■ **ABSTRACT:** The nucleus basalis of Meynert was examined in six patients with Alzheimer's disease and five age-matched controls. A cytoarchitectonic study was followed by quantitative analysis of the population of neurons and by the determination of their nuclear area. Confirming previous neuropathological observations in Alzheimer's disease, a neuronal loss of 43% in the anterior, 25% in the intermediate and 30.5% in the posterior subdivisions of the nucleus basalis of Meynert was observed. Numerous surviving cells showed neurofibrillary tangles. In addition, we found that the nuclear area of the remaining nucleus basalis of Meynert neurons was significantly increased in all three subdivisions by at least 16%. The combined observation of cell loss and nuclear hypertrophy suggests that both regenerative and degenerative changes coexist in the nucleus basalis in Alzheimer's disease.

POLARITY OF IMMUNOGENS: IMPLICATIONS FOR VACCINE DESIGN*

■ José Golvano, Juan J. Lasarte, Pablo Sarobe, Arturo Gullón, Jesús Prieto and Francisco Borrás-Cuesta. Departamento de Medicina Interna and Departamento de Genética, Universidad de Navarra, Pamplona. Eur. J. Immunol. 1990. 20: 2.363-2.366. ■ Peptide constructs have been engineered consisting of amino acid sequence determinant recognized by T cells (TD) co-linearly linked to haptenic peptides. It was found that high anti-hapten antibody titers were induced after immunization with those constructs which had the TD sequence in the N-terminal position with respect to the hapten. Low or zero titers were elicited when the TD was in C-terminal position. Also, a high anti-hapten antibody titer corresponded to a low or zero anti-TD antibody titer and viceversa. These results suggest that immunogens are polar and stress the relevance of searching the more adequate position of the TD within a peptide construct when designing immunogens or synthetic peptide vaccines.

MONOCYTE DISORDER CAUSING CELLULAR IMMUNODEFICIENCY: A FAMILY STUDY

■ J. Prieto, M. L. Subirá, A. Castilla, M. L. Civeira and M. Serrano. Centre for Biomedical Research. Departments of Internal Medicine and Immunology. Clinica Universitaria, University of Navarra Pamplona, Spain. Clin. Exp. Immunol. (1990) 79, 1-6. ■ **SUMMARY:** We report a familial type of monocyte dysfunction not recognized previously. This disorder was observed in a young adult man with a long clinical history of recurrent, self-limited episodes of cryptogenic fever accompanied by digestive and respiratory symptoms and repeated oral and skin infections. Lectin-induced lymphocyte transformation was reduced and skin tests revealed energy to cytoskeletal vimentin intermediate filaments, HLA-Dr antigens and immunological receptors for IgG Fc and C3b. These abnormal monocytes demonstrated impaired phagocytosis and reduced activating factors by these cells was found to be defective. Lymphocytes from the patient responded appropriately to lectin in the presence of normal monocytes. Two family members of the proband presented similar monocyte defects although they only manifested minor clinical symptoms. This syndrome underlines the interest of testing monocyte markers and function in subjects with clinical manifestations of immunodeficiency. ■ **Keywords:** Monocyte dysfunction, familial immunodeficiency, intermediate filaments, fever.

PLACEBO-CONTROLLED TRIAL OF NIMODIPINE IN THE TREATMENT OF ACUTE ISCHEMIC CEREBRAL INFARCTION

■ Eduardo Martínez-Vila, M. D.; Francisco Guillén, M. D.; José A. Villanueva, M. D.; Jordi Matías-Guiu, M. D.; Joan Bigorra, M. D.; Pedro Gil, M. D.; Antoni Carbonell, M. D., and José M. Martínez-Lage, M. D. (Stroke 1990; 21:1.023-1.028). ■ Nimodipine is a 1,4-dihydropyridine derivative that shows a preferential cerebrovascular activity in experimental animals. Clinical data suggest that nimodipine has a beneficial effect on the neurologic outcome of patients suffering an acute ischemic stroke. Our double-blind placebo-controlled multicenter trial was designed to assess the effects of oral nimodipine on the mortality rate and neurologic outcome of patients with an acute ischemic stroke. One hundred sixty-four patients were randomly allocated to receive either nimodipine tablets (30 mg. q. i. d.) or identical placebo tablets for 28 days. Treatment was always started ≤ 48 hours after the acute event. The Mathew Scale, slightly modified by Gelmers et al., was used for neurologic assessment. Mortality rate and neurologic outcome after 28 days were used as evaluation criteria. We considered 123 patients to be valid for the analysis of efficacy. Mortality rates did not differ significantly between groups. Neurologic outcome after 28 days of therapy did not differ significantly between groups. However, when only those patients most likely to benefit from any intervention (Mathew Scale sum score of ≤ 65 at baseline) were analyzed separately in post hoc-defined subgroups, the nimodipine-treated subgroup showed a significantly better neurologic outcome. This result suggests that some patients with acute ischemic stroke will benefit from treatment with nimodipine tablets.