

Resúmenes de Publicaciones

CHRONIC INFLAMMATION AS A MANIFESTATION OF DEFECTS IN IMMUNOREGULATORY NETWORKS: IMPLICATIONS FOR NOVEL THERAPIES BASED ON MICROBIAL PRODUCTS.

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Based on a unifying theory presented here, it is predicted that the immune defects resulting in chronic inflammation rather than effective immune responses could be rectified by the therapeutic use of agents prepared from micro-organisms. With appropriate molecular patterns, these should be able to induce protective immunoregulatory networks or to reprogramme defective ones. In contrast to acute inflammation, chronic inflammation appears to have no beneficial role, but is a state of sustained immune reactivity in the presence or progression of a disease process. This results in an escalating cycle of tissue damage followed by unproductive tissue repair, breaks in self-tolerance, malignant transformation or deleterious changes in tissue morphology and function. Such inappropriate immune reactivity is an underlying characteristic, either in initiation or maintenance, of a diverse range of disease states including chronic infection, autoimmunity, allergy, cancer, vascular disease and metabolic alterations. Evidence is presented that the inappropriate immune reactivity is due, at least to some extent, to failures in the establishment of immunoregulatory networks as a result of hygiene-related factors. Such networks are the result of activation of antigen-presenting cells, principally dendritic cells, by molecular patterns of micro-organisms encountered sequentially during life and establishing the 'biography' of the immune system.

Inflammopharmacol 17: 193-203, 2009

SHORT TREATMENT WITH THE TUMOUR NECROSIS FACTOR-ALPHA BLOCKER INFlixIMAB DIMINISHES CHRONIC CHAGASIC MYOCARDITIS IN RATS WITHOUT EVIDENCE OF TRYPANOSOMA CRUZI REACTIVATION.

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Tumour necrosis factor (TNF)-alpha is crucial for resistance to *Trypanosoma cruzi* acute infection, but there is scant information on its role during the chronic phase. To address this issue, we analysed whether a short treatment with a TNF- α blocker affected the course and characteristics of chronic disease in a rat experimental model of *T. cruzi* infection. An anti-TNF-alpha agent (influximab) was administered during the chronic phase for a period of 4 weeks (3 mg/kg/week), while control infected rats were inoculated with saline physiological solution. Search for parasites yielded non-successful results in all infected groups, irrespective of treatment. Nevertheless, the presence of *T. cruzi* kDNA in heart tissue was detected in infected and infected plus treated animals. Because influximab might induce changes in the anti-parasite cytokine response, circulating levels of interleukin (IL)-10, interferon-gamma and nitric oxide were evaluated. An increase in IL-10 levels was observed only in the infected group treated with the anti-TNF-alpha blocker compared to the remaining groups ($P < 0.05$). A clear attenuation of histological damage associated with a diminution of cardiac TNF-alpha mRNA expression was observed in the

infected and treated animals compared to the infected and non-treated group. Blocking of TNF-alpha during a relatively short period in chronically infected rats did not lead to evident parasite reactivation but reduced myocarditis severity significantly, indicating a role of this cytokine in the pathogenesis of chronic myocardial damage.

Clin Experiment Immunol 157: 291-9, 2009.

THE IMPACT OF INFECTIOUS DISEASES UPON NEUROENDOCRINE CIRCUITS.

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During infectious diseases, neuroendocrine and immune networks act in concert, facilitating host response. It is known that infections cause profound immune changes, but the impact upon immunoendocrine circuits has been less studied. Disorders in the hypothalamic-pituitary-adrenal (HPA) axis were frequently observed associated with infections, and these changes often occur in parallel to alterations in the systemic cytokine network. Explanations for the infection-associated immunoendocrine disturbances include several and not mutually exclusive possibilities. Changes in cytokine levels can enhance or suppress the HPA axis, by acting at the hypothalamus-pituitary unit and/or at the adrenal glands. In situ inflammatory reactions or structural changes like vascular alterations or an enhanced extracellular matrix deposition in the endocrine microenvironment may also lead to a transient HPA dysfunction. Lastly, a microbe-related effect by means of pathogen infiltration or exploitation of the host's hormonal microenvironment may be involved as well. A better understanding of the relevance of immunoendocrine communication during infectious diseases, and how disturbances in the flux of information lead to neuroendocrine immune-related disorders will provide important insights into mechanisms underlying the disease pathology.

Neuroimmunomodulation 16: 96-105, 2009.

BONE MASS AND GEOMETRY OF THE TIBIA AND THE RADIUS OF MASTER SPRINTERS, MIDDLE AND LONG DISTANCE RUNNERS, RACE-WALKERS AND SEDENTARY CONTROL PARTICIPANTS: A PQCT STUDY

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Mechanical loading is thought to be a determinant of bone mass and geometry. Both ground reaction forces and tibial strains increase with running speed. This study investigates the hypothesis that surrogates of bone strength in male and female master sprinters, middle and long distance runners and race-walkers vary according to discipline-specific mechanical loading from sedentary controls. Bone scans were obtained by peripheral Quantitative Computed Tomography (pQCT) from the tibia and from the radius in 106 sprinters, 52 middle distance runners, 93 long distance runners and 49 race-walkers who were competing at master championships, and who were aged between 35 and 94 years. Seventy-five age matched, sedentary people served as control group. Most athletes of this study had started to practice their athletic discipline after the age of 20, but the current training regime had typically been maintained for more than a decade. As hypothesised, tibia diaphyseal bone mineral

content (vBMC), cortical area and polar moment of resistance were largest in sprinters, followed in descending order by middle and long distance runners, race-walkers and controls. When compared to control people, the differences in these measures were always N13% in male and N23% in female sprinters (pb0.001). Similarly, the periosteal circumference in the tibia shaft was larger in male and female sprinters by 4% and 8%, respectively, compared to controls (p<0.001). Epiphyseal group differences were predominantly found for trabecular vBMC in both male and female sprinters, who had 15% and 18% larger values, respectively, than controls (pb0.001). In contrast, a reverse pattern was found for cortical vBMD in the tibia, and only few group differences of lower magnitude were found between athletes and control people for the radius. In conclusion, tibial bone strength indicators seemed to be related to exercise-specific peak forces, whilst cortical density was inversely related to running distance. These results may be explained in two, non-exclusive ways. Firstly, greater skeletal size may allow larger muscle forces and power to be exerted, and thus bias towards engagement in athletics. Secondly, musculoskeletal forces related to running can induce skeletal adaptation and thus enhance bone strength.

Bone 45: 91-7, 2009.

VOLUMETRIC BMD VALUES OF ARCHAEOLOGICAL HUMAN BONE REMAINS WITH PQCT AND DEXA

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Bone mineral density (BMD) is a mediating factor of some attritional taphonomic processes. In the last few decades BMD has been successfully employed to assess differential preservation in faunal archaeological samples. In contrast, the BMD of human remains was scarcely studied with taphonomic purposes. Moreover, there is some controversy concerning the reliability of the methods proposed to evaluate this bone property. In this study, we determined the human postcranial volumetric BMD (vBMD) of an archaeological assemblage from Tierra del Fuego (Argentina), with peripheral quantitative computed tomography (pQCT) and area BMD with X-ray densitometry (DEXA). Although the pQCT-assessed vBMD values were more accurate and offer important biomechanical references, the information given by the shape-adjusted vBMD values calculated from DEXA aBMD data is also reliable and provides enough resolution for detection of BMD-related taphonomic processes.

J Taphonomy 7: 29-45, 2009.

PROTEÍNA C REACTIVA COMO FACTOR PRONÓSTICO DE MORTALIDAD EN LA UNIDAD DE CUIDADOS INTENSIVOS.

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Objetivo: Determinar el valor pronóstico de la proteína C reactiva (PCR) y correlacionarla con la puntuación APACHE II en pacientes ingresados a una Unidad de Cuidados Intensivos (UCI).

Diseño: Cohorte retrospectiva.

Pacientes: Se estudiaron 879 pacientes ingresados a la UCI por cualquier causa durante 2 años y que permanecieron al menos 24 horas.

Método: Se determinó el nivel de PCR al ingreso y se calculó a su vez la puntuación APACHE II a las 24

horas. Los valores de PCR fueron correlacionados con la puntuación APACHE II junto con otras variables (sexo, edad, patología de ingreso, días de ingreso).

Resultados: Los niveles de PCR más altos se obtuvieron de los sujetos que ingresaron por patología infecciosa o shock séptico-fallo multiorgánico. Los pacientes con valores de PCR > 10 mg/dL presentaron un promedio de edad y puntuación APACHE II mayores, permanecieron internados por más tiempo y la mortalidad fue más elevada ($p < 0,0001$). El valor predictivo de muerte fue mayor a medida que aumentaron los valores de PCR, con una especificidad del 72,3% cuando la cifra superaba los 10 mg/dL.

Conclusiones: La PCR constituye un marcador evolutivo precoz, específico y de bajo costo, cualidades que permiten proponerlo como examen rutinario al ingreso de los pacientes a la UCI.

Med Intensiva 32:424-30, 2008.