

Cuban Research in Current International Journals

The following selection—alphabetical by title—reflects Cuban publishing in international medical and population health journals over the last quarter on an array of topics. Links to these journal articles may be found at www.medicc.org/mediccreview.

A Comprehensive Review of Spinocerebellar Ataxia Type 2 in Cuba. Velázquez-Pérez L, Rodríguez-Labrada R, García-Rodríguez JC, Almaguer-Mederos LE, Cruz-Mariño T, Laffita-Mesa JM. *Cerebellum*. 2011 Mar 12. [Epub ahead of print]

Spinocerebellar ataxia type 2 (SCA2) is an autosomal dominant cerebellar ataxia characterized by a progressive cerebellar syndrome associated to saccadic slowing, peripheral neuropathy, cognitive disorders, and other multisystem features. SCA2 is caused by the abnormal expansion of cytosine-adenine-guanine triplet repeats in the encoding region of the ATXN2 gene and therefore the expression of toxic polyglutamine expansions in the ataxin 2 protein, which cause progressive neuronal death of Purkinje cells in the cerebellum and several pontine, mesencephalic, and thalamic neurons among other cells. Worldwide, SCA2 is the second most frequent type of spinocerebellar ataxia, only surpassed by SCA3. Nevertheless, in Holguin, Cuba, the disease reaches the highest prevalence, resulting from a putative foundational effect. This review discusses the most important advances in the genotypical and phenotypical studies of SCA2, highlighting the comprehensive characterization reached in Cuba through clinical, neuroepidemiological, neurochemical, and neurophysiological evaluation of SCA2 patients and pre-symptomatic subjects, which has allowed the identification of new disease biomarkers and therapeutical opportunities. These findings provide guidelines, from a Cuban viewpoint, for the clinical management of the disease, its diagnosis, genetic counseling, and therapeutical options through rehabilitative therapy and/or pharmacological options.

Comparison of major immunoglobulin intrathecal synthesis patterns in Ecuadorian and Cuban patients with angiostrongyliasis. Padilla-Docal B, Dorta-Contreras AJ, Moreira JM, Martini-Robles L, Muzzio-Aroca J, Alarcón F, et al. *Am J Trop Med Hyg*. 2011 Mar;84(3):406–10.

Angiostrongylus cantonensis meningitis was first reported in Cuba in 1981, and it was recently reported in South America. The aim of this paper is to evaluate the intrathecal immunoglobulin synthesis patterns from Cuba's and Ecuador's patients with angiostrongyliasis; 8 Ecuadorian patients from two different outbreaks and 28 Cuban patients were studied. Simultaneous blood and cerebrospinal fluid samples were taken. Immunoglobulin (Ig) A, IgM, IgG, and albumin were quantified by radial immuno-

diffusion. Corresponding Reibergrams were applied. A three-Ig pattern was the most frequent in the two groups, but IgM was present in all Ecuadorian young mature patients; however, in the Cuban children, only 12 of 28 patients had intrathecal IgM, but about 90% had an IgA and IgG synthesis at time of later puncture. This indicates that, with a larger amount of parasites ingested, clinical symptoms are more severe, and a higher frequency of intrathecal IgM synthesis could be observed. This is discussed as a similarity with the intrathecal IgM synthesis in African trypanosomiasis.

Device-associated infection rates in adult intensive care units of Cuban university hospitals: International Nosocomial Infection Control Consortium (INICC) findings. Guache-Garcel H, Requeijo-Pino O, Rosenthal VD, Morales-Pérez C, Delgado-González O, Fernández-González D. *Int J Infect Dis*. 2011 Mar 28;15(5):e357–62.

Objectives To determine the rate of device-associated healthcare-associated infection (DA-HAI), microbiological profile, length of stay (LOS), extra mortality, and hand hygiene compliance in two intensive care units (ICUs) of two hospital members of the International Infection Control Consortium (INICC) of Havana, Cuba. **Methods** An open label, prospective cohort, active DA-HAI surveillance study was conducted on adults admitted to two tertiary-care ICUs in Cuba from May 2006 to December 2009, implementing the methodology developed by INICC. Data collection was performed in the participating ICUs, and data were uploaded and analyzed at the INICC headquarters on proprietary software. DA-HAI rates were registered by applying the definitions of the US Centers for Disease Control and Prevention National Healthcare Safety Network (CDC NHSN). We analyzed the mechanical ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLA-BSI), and catheter-associated urinary tract infection (CAUTI) rates, microorganism profile, extra length of stay (ELOS), extra mortality, and hand hygiene compliance. **Results** During 14512 days of hospitalization, 1982 patients acquired 444 DA-HAIs, an overall rate of 22.4% (95% CI 20.6–24.3) or 30.6 (95% CI 27.8–33.5) DA-HAIs per 1000 ICU-days. The CLA-BSI rate was 2.0 (95% CI 1.2–3.1) per 1000 central line-days, the VAP rate was 52.5 (95% CI 47.2–58.3) per 1000 ventilator-days, and the CAUTI rate was 8.1 (95% CI 6.5–10.0) per 1000 catheter-days. LOS of patients was 4.9 days for those without DA-HAI, 23.3 days for those with CLA-BSI, and 23.8 days for those with VAP.

CAUTI LOS was not calculated due to the lack of data. Extra mortality was 47% (relative risk (RR) 2.42; $p=0.0693$) for VAP and 17% (RR 1.52; $p=0.5552$) for CLA-BSI. The only patient with CAUTI died, but there was too little mortality data regarding this infection type to consider this significant. *Escherichia coli* was the most commonly isolated microorganism. The overall hand hygiene compliance was 48.6% (95% CI 42.8–54.3). **Conclusions** DA-HAI rates, LOS, and mortality were found to be high, and hand hygiene low. It is of primary importance that infection control programs that include outcome and process surveillance are implemented in Cuba.

Emotional Tagging—A Simple Hypothesis in a Complex Reality. Bergado JA, Lucas M, Ritcher-Levin G. *Prog Neurobiol*. 2011 Mar 21. [Epub ahead of print].

At the psychological level, the notion that emotional events may be better remembered is a long accepted view. Its translation into neurobiological mechanisms has led to the proposal of the 'Emotional Tag' concept, according to which, the activation of the amygdala by emotionality would result in modulation of neural plasticity in brain regions (e.g. hippocampus) involved in forming memory of the emotional event. In line with this idea, amygdala activation (by electrical stimulation or exposure to an emotional event), has been demonstrated to affect synaptic plasticity in the hippocampus. Furthermore, the mechanisms associated with the formation of a 'Synaptic Tag', which is a mechanism proposed to explain the specificity of synaptic plasticity, could subserve the effects of the 'Emotional Tag' on synaptic plasticity in the hippocampus. The literature reviewed here supports this view but points also to additional factors that should be taken into consideration, such as intensity, duration, controllability of the emotional experience, age of exposure and relations between the emotional aspects of the experience and the event-to-be-remembered. These factors do not only affect the behavioral outcome of the stressful experience but also find their expression in variations in the neuronal and biochemical pathways that are activated, and in the way those will interact with memory formation mechanisms. While adding complexity to the notion of the 'Emotional Tag', taking such factors into consideration is likely to bring us closer to elucidating the neural mechanisms involved in emotional memory modulation and to our understanding of the neurobiology of associated disorders, such as PTSD.

Evidence on impact of community-based environmental management on dengue transmission in Santiago de Cuba. Toledo ME, Rodríguez A, Valdés L, Carrión R, Cabrera G, Banderas D, et al. *Trop Med Int Health*. 2011 Mar 21. doi: 10.1111/j.1365-3156.2011.02762.x. [Epub ahead of print]

During the dengue outbreak that struck Santiago de Cuba in 2006–2007, we conducted an observational study in the Mariana Grajales district, the former setting of a community trial for *Aedes aegypti* control. In the trial, community working groups (CWG) had been created in 29 randomly selected intervention house blocks, and routine vector control activities alone were conducted in the remaining 30 control blocks. The CWG elaborated and implemented with the population plans and activities to reduce *Aedes* infestation. They were still functional in 2006 and continued organizing community-based environmental management activities. The attack rate of dengue fever during the outbreak was 8.5 per 1000 inhabitants in the former intervention blocks and 38.1 per 1000 inhabitants in the control blocks, which corresponds to a relative risk of 4.5 (95% CI 3.1–6.5). There was a significantly higher proportion of unaffected intervention blocks, and affected blocks had, on average, substantially fewer cases than affected control blocks. This study indicates that community-based environmental management inserted in the routine *A. aegypti* control programme can not only sustainably curb vector infestation but also have an impact on dengue transmission.

Fatal 2009 pandemic influenza A (H1N1) in a bone marrow transplant recipient. Abdo A, Alfonso C, Díaz G, Wilford M, Rocha M, Verdecia N. *J Infect Dev Ctries*. 2011 Mar 2;5(2):132–7.

Conditions characterized by immunosuppression have been recently reported as risk factors for severe novel swine-origin influenza A (H1N1) virus (S-OIV) infection during the current 2009 pandemic. We report clinical and virological findings, antiviral therapy, and post-mortem study of S-OIV in an adult bone marrow transplant recipient. The viral genome was amplified by real-time reverse transcriptase polymerase chain reaction (RT-PCR) from a nasopharyngeal swab specimen. The patient developed acute respiratory distress syndrome, septic shock, and eventually succumbed with a severe pulmonary haemorrhage. To the best of our knowledge, the entire clinical/therapy management and pathological examination in a transplant recipient infected with the S-OIV has not been previously documented. The fatal ending in this bone marrow transplant recipient supports recommendations that call for education measures, S-OIV vaccination, early diagnosis and aggressive treatment in the transplant population.

From Blood Oxygenation Level Dependent (BOLD) Signals to Brain Temperature Maps. Sotero RC, Iturria-Medina Y. *Bull Math Biol*. 2011 Mar 16. [Epub ahead of print]

A theoretical framework is presented for converting Blood Oxygenation Level Dependent (BOLD) images to brain temperature maps, based on the idea that disproportional local changes in cerebral blood flow (CBF) as compared with cerebral metabolic rate of oxygen consumption (CMRO (2)) during functional brain activity, lead to both brain temperature changes and the BOLD effect. Using an oxygen limitation model and a BOLD signal model, we obtain a transcendental equation relating CBF and CMRO (2) changes with the corresponding BOLD signal, which is solved in terms of the Lambert W function. Inserting this result in the dynamic bioheat equation describing the rate of temperature changes in the brain, we obtain a nonautonomous ordinary differential equation that depends on the BOLD response, which is solved numerically for each brain voxel. Temperature maps obtained from a real BOLD dataset registered in an attention to visual motion experiment were calculated, obtaining temperature variations in the range: (-0.15 to 0.1) which is consistent with experimental results. The statistical analysis revealed that significant temperature activations have a similar distribution pattern than BOLD activations. An interesting difference was the activation of the precuneus in temperature maps, a region involved in visuospatial processing, an effect that was not observed on BOLD maps. Furthermore, temperature maps were more localized to gray matter regions than the original BOLD maps, showing less activated voxels in white matter and cerebrospinal fluid.

Interactions between genetic admixture, ethnic identity, APOE genotype and dementia prevalence in an admixed Cuban sample; a cross-sectional population survey and nested case-control study. Teruel BM, Rodríguez JJ L, McKeigue P, Mesa TT C, Fuentes E, Cepero A AV, et al. *BMC Med Genet*. 2011 Mar 24;12(1):43.

Background The prevalence and incidence of dementia are low in Nigeria, but high among African-Americans. In these populations there is a high frequency of the risk-conferring APOE-ε4 allele, but the risk ratio is less than in Europeans. In an admixed population of older Cubans we explored the effects of ethnic identity and genetic admixture on APOE genotype, its association with dementia, and dementia prevalence. **Methods** A cross-sectional catchment area survey of 2928 residents aged 65 and over, with a nested case-control study of individual admixture. Dementia diagnosis was established using 10/66 Dementia and DSM-IV criteria. APOE genotype was determined in 2520 participants, and genetic admixture in 235 dementia cases and 349 controls. **Results** Mean African admixture proportions were 5.8% for white, 28.6% for mixed and 49.6% for black ethnic identities. All three groups were substantially admixed with considerable overlap. African admixture was linearly related to number of APOE-ε4 alleles. One or more APOE-ε4 alleles was associated with dementia in white

and black but not mixed groups but neither this, nor the interaction between APOE-ε4 and African admixture (PR 0.52, 95% CI 0.13–2.08) were statistically significant. Neither ethnic identity nor African admixture was associated with dementia prevalence when assessed separately. However, considering their joint effects African versus European admixture was independently associated with a higher prevalence, and mixed or black identity with a lower prevalence of dementia. **Conclusions** APOE genotype is strongly associated with ancestry. Larger studies are needed to confirm whether the concentration of the high-risk allele in those with African ancestry is offset by an attenuation of its effect. Counter to our hypothesis, African admixture may be associated with higher risk of dementia. Although strongly correlated, effects of admixture and ethnic identity should be distinguished when assessing genetic and environmental contributions to disease risk in mixed ancestry populations.

Interrelationship between myocardial perfusion imaging, coronary calcium score, and endothelial function in asymptomatic diabetics and controls. Peix A, Cabrera LO, Heres F, Rodríguez L, Valdés A, Valiente J, et al. *J Nucl Cardiol*. 2011 Mar 24. [Epub ahead of print]

Background Coronary artery disease is a leading cause of death among diabetics, and silent ischemia is a major concern in patients with diabetes mellitus (DM). **Methods** To detect the prevalence of ischemia in diabetics by myocardial perfusion imaging (MPI), and compare it to a control group without DM but with coronary risk factors, as well as to explore the relationship between silent ischemia, endothelial dysfunction, and coronary calcium, 59 patients (Group I) and 42 controls (Group II) were included. All underwent clinical and laboratory evaluations, gated MPI, brachial artery vasodilation measured by ultrasonography, and coronary calcium score (CCS). **Results** Twenty diabetics showed perfusion defects, vs seven controls (p=0.04). There was no significant difference between both groups regarding the brachial artery vasodilator responsiveness: 4.49%±4.26% (diabetics) vs 4.70%±4.98% (controls). Mean CCS was 74 in diabetics vs 5 in controls (p=0.01). The only risk factor significantly associated with an abnormal MPI was the presence of diabetes (p=0.03). In the whole population of patients and in diabetics, the abnormal endothelium-dependent vasodilation, the CCS >100, and the cholesterol/HDL ratio >4, showed an OR >1. CCS exhibited the higher OR among the whole population: OR 2.15 (95% CI 0.42–10.99); while for diabetics it was the cholesterol/HDL ratio: OR 3.95 (95% CI 0.71–21.84). **Conclusions** Reversible perfusion defects and coronary calcium are more frequent in diabetics. CCS, abnormal endothelium-dependent vasodilation, and cholesterol/HDL ratio higher than 4, showed an association with perfusion abnormalities in asymptomatic diabetics. 