

## Cuban Research in Current International Journals

The following selection – alphabetical by title - reflects Cuban medical publishing in international journals over the last quarter on an array of topics. Links to these journal articles may be found at [www.medicc.org/mediccreview](http://www.medicc.org/mediccreview).

### Association of atopy, asthma, allergic rhinoconjunctivitis, atopic dermatitis and intestinal helminth infections in Cuban children.

Wördemann M, Junco Díaz R, Menocal Heredia L, Collado Madruga AM, Ruiz Espinosa A, Cordovi Prado R, et al. *Trop Med Int Health*. 2008 Mar;13(2):180-186.

**Objective** To examine the relationship of past and current intestinal helminth infections with asthma, allergic rhinoconjunctivitis, atopic dermatitis and atopy. **Methods** Cross-sectional study of 1,320 children aged 4–14 years from two Cuban municipalities. Helminth infections were determined by stool examination and parental questionnaire. Asthma, rhinoconjunctivitis and atopic dermatitis were diagnosed by International Study of Asthma and Allergies in Childhood questionnaire, asthma additionally by spirometry, atopy by skin prick testing. **Results** Questionnaire-based frequencies were 21% for asthma, 14% for allergic rhinoconjunctivitis and 8% for atopic dermatitis. According to spirometry, 4% had asthma; 20% had a positive skin prick test. A history of infection for *Enterobius vermicularis* was associated with increased risk of atopic dermatitis (OR 1.88,  $P = 0.001$ ) and allergic rhinoconjunctivitis (OR 1.34,  $P = 0.046$ ), and hookworm with increased risk of allergic rhinoconjunctivitis (OR 2.77,  $P = 0.021$ ). A positive stool examination for *Ascaris lumbricoides* infection was negatively associated with atopic dermatitis (OR 0.22,  $P = 0.007$ ). Asthma and atopy were unrelated to helminth infections. **Conclusion** Current *A. lumbricoides* infection protects against atopic dermatitis in Cuban children, while past infection with *E. vermicularis* and hookworm are risk factors for allergic rhinoconjunctivitis and/or atopic dermatitis. Apparently, interactions differ depending on the type of helminth and atopic disease and on the time of helminth infestation.

### Behavioral and antiepileptic effects of acute administration of the extract of the plant *Cestrum nocturnum* Lin (lady of the night).

Pérez-Saad H, Buznego MT. *Epilepsy Behav*. 2008 Apr;12(3):366-372.

*Cestrum nocturnum* is a garden shrub from the family *Solanaceae* and is used as a remedy for different health disorders. The aim of the present work was to investigate the potential neuropharmacological action profile of decoctions obtained from dry leaves of the plant. Decoctions were tested in different neurophar-

macological models—Irwin test, exploratory behavior, tests for analgesia, isoniazid- and picrotoxin-induced convulsions, and maximal electroshock seizures—in mice, as well as in amphetamine-induced stereotypies and penicillin epileptic foci in rats. Decoctions of 1 and 5% (D1 and D5) induced restlessness, and the 30% decoction (D30) induced passivity. D5 and D30 reduced significantly exploratory behavior and amphetamine-induced stereotypies within a 3-hour observation period. The latter effect was apparent during the second 60 minutes. Decoctions reduced the amount of writhes induced by acetic acid in a dose-dependent manner, but were not effective in the hot plate model. The decoctions were not effective against pharmacologically induced convulsions. However, repeated administration of five doses of D5, at 1-hour intervals, reduced the amplitude of penicillin-induced epileptic spikes in both primary and secondary foci, in curarized rats. Taken together, the results suggest that *C. nocturnum* possesses active substances with analgesic activity provided through a peripheral action mechanism, in parallel with some psychoactive activity that does not fit well the neuropharmacological action profile of known reference neurotropic drugs.

### Could clinical audit improve the diagnosis of pulmonary tuberculosis in Cuba, Peru and Bolivia?

Siddiqi K, Volz A, Armas L, Otero L, Ugaz R, Ochoa E, et al. *Trop Med Int Health*. 2008 Apr;13(4):566–578.

**Objectives** To assess the effectiveness of clinical audit in improving the quality of diagnostic care provided to patients suspected of tuberculosis; and to understand the contextual factors which impede or facilitate its success. **Methods** Twenty-six health centres in Cuba, Peru and Bolivia were recruited. Clinical audit was introduced to improve the diagnostic care for patients attending with suspected TB. Standards were based on the WHO and TB programme guidelines relating to the appropriate use of microscopy, culture and radiological investigations. At least two audit cycles were completed over 2 years. Improvement was determined by comparing the performance between two six-month periods pre- and post-intervention. Qualitative methods were used to ascertain facilitating and limiting contextual factors influencing change among healthcare professionals' clinical behaviour after the introduction of clinical audit. **Results** We found a significant improvement in 11 of 13 criteria in Cuba, in 2 of 6 criteria in Bolivia and in 2 of 5 criteria in Peru. Twelve out

of 24 of the audit criteria in all three countries reached the agreed standards. Barriers to quality improvement included conflicting objectives for clinicians and TB programmes, poor coordination within the health system and patients' attitudes towards illness. **Conclusions** Clinical audit may drive improvements in the quality of clinical care in resource-poor settings. It is likely to be more effective if integrated within and supported by the local TB programmes. We recommend developing and evaluating an integrated model of quality improvement including clinical audit.

### Intracluster correlation coefficients from the 2005 WHO Global Survey on Maternal and Perinatal Health: implications for implementation research.

Taljaard M, Donner A, Villar J, Wojdyla D, Velazco A, Bataglia V, et al. *Paediatr Perinat Epidemiol*. 2008 Mar;22:117–125.

Cluster-based studies involving aggregate units such as hospitals or medical practices are increasingly being used in healthcare evaluation. An important characteristic of such studies is the presence of intracluster correlation, typically quantified by the intracluster correlation coefficient (ICC). Sample size calculations for cluster-based studies need to account for the ICC, or risk underestimating the sample size required to yield the desired levels of power and significance. In this article, we present values for ICCs that were obtained from data on 97,095 pregnancies and 98,072 births taking place in a representative sample of 120 hospitals in eight Latin American countries. We present ICCs for 86 variables measured on mothers and newborns from pregnancy to the time of hospital discharge, including 'process variables' representing actual medical care received for each mother and newborn. Process variables are of primary interest in the field of implementation research. We found that overall, ICCs ranged from a minimum of 0.0003 to a maximum of 0.563 (median 0.067). For maternal and newborn outcome variables, the median ICCs were 0.011 (interquartile range 0.007–0.037) and 0.054 (interquartile range 0.013–0.075) respectively; however, for process variables, the median was 0.161 (interquartile range 0.072–0.328). Thus, we confirm previous findings that process variables tend to have higher ICCs than outcome variables. We demonstrate that ICCs generally tend to increase with higher prevalences (close to 0.5). These results can help researchers calculate the required sample size for future research studies in maternal and perinatal health.

### Promoting health in response to global tourism expansion in Cuba.

Spiegel JM, González M, Cabrera GJ, Catusus S, Vidal C, Yassi A. *Health Promot Int*. 2008 Mar;23(1):60-9. Epub 2007 Dec 14.

The ability of communities to respond to the pressures of globalization is an important determinant of community health. Tourism is a rapidly growing industry and there is an increasing concern about its health impact on local communities. Nonetheless, little research has been conducted to identify potential mitigating measures. We therefore took advantage of the 'natural experiment' provided by the expansion of tourism in Cuba, and conducted four focus groups and key informants interviews in each of two coastal communities. Participants expressed concerns about psycho-social impacts as well as occupational and environmental concerns, and both infectious and chronic diseases. A wide array of programs that had been developed to mitigate potential negative were described. Some of the programs were national in scope and others were locally developed. The programs particularly targeted youth as the most vulnerable population at risk of addictions and sexually transmitted infections. Occupational health concerns for workers in the tourism sector were also addressed, with many of the measures implemented protecting tourists as well. The health promotion and various other participatory action initiatives implemented showed a strong commitment to address the impacts of tourism and also contributed to building capacity in the two communities. Although longitudinal studies are needed to assess the sustainability of these programs and to evaluate their long-term impact in protecting health, other communities can learn from the initiatives taken.

### National Prevalence of Nosocomial Infections. Cuba 2004.

Izquierdo-Cubas F, Zambrano A, Frómeta I, Gutiérrez A, Bastanzuri M, Guanache H, et al. *J Hosp Infect*. 2008 Mar;68(3):234-240.

In 1983 Cuba instituted its first Nosocomial Infection (NI) Control and Prevention National Program with a continuous surveillance system. We undertook the first NI prevalence study in 1997 in an attempt to compare our national findings with international results. A second prevalence study with a randomised design was undertaken between 24 and 29 May 2004. The overall rate of NI was 7.3% (284/4240; 95% CI: 5.9–7.4), and 6.7% of patients were found to have at least one NI. The highest rates were found in intensive care, intermediate care and burn units. The most frequent NI was surgical site infection, whereas the number of urinary tract infections remained low. Microbiological culture was obtained in nearly 53% of infections; *Staphylococcus aureus* and *Pseudomonas* spp. were the most commonly isolated pathogens. Cephalosporins and aminoglycosides were the antibiotics most

often used in the treatment of NIs. The risk factors for NIs found in the Cuban studies were similar to international reports.

### Obesity reduction and its possible consequences: what can we learn from Cuba's Special Period? (Commentary)

Franco M, Ordúñez P, Caballero B, Cooper RS. *Can Med Assoc J*. 2008 Apr;178(8):1032-4.

(No abstract available; first 300 words provided). In a recent issue of the *American Journal of Epidemiology*, we described the relation between sustained population-wide weight loss and a decline in all-cause mortality and in the rates of death from diabetes mellitus and cardiovascular disease in Cuba. The widespread weight loss resulted from the economic crisis known as the "Special Period," which Cuba experienced in the 1990s after the collapse of the Soviet Union. This period of economic and social hardship also had negative consequences for health. For example, a neuropathy outbreak, possibly due to vitamin deficiencies, affected 50 000 people between 1992 and 1993, and the decline in infant mortality that Cuba had been experiencing reversed between 1990 and 1993. The neuropathy outbreak did not affect children, elderly people or pregnant women because a special rationing system was in place to protect them. The Cuban population showed high levels of social cohesion, especially within families, in a time of economic hardship. During this Special Period, per capita daily energy intake fell from 2899 kcal (12 180 kJ) to 1863 kcal (7820 kJ), and energy expenditure increased because fuel shortages led people to walk or ride their bicycles rather than use public transportation. The proportion of physically active adults increased from 30% to 67%. Population-representative studies in Cienfuegos, Cuba, in 1991 and 1995 showed a 1.5-unit decrease in the body mass index. The prevalence of obesity declined from 14% to 7%, the prevalence of overweight increased from 26% to 27%, and the prevalence of normal weight increased from 60% to 66%. The decline in body weight in the population represents a modest weight loss of 4–5 kg, or 5%–6% of body weight per adult. In subsequent years, rates of death decreased markedly from 1997 to 2002: by 51% for diabetes, 35% for coronary artery disease, 20% for stroke and 18% for all-cause mortality.

### Predicting functional residues in Plasmodium falciparum plasmepsins by combining sequence and structural analysis with molecular dynamics simulations.

Valiente PA, Batista PR, Pupo A, Pons T, Valencia A, Pascutti PG. *Proteins*. 2008 Apr 28.

Plasmepsins are aspartic proteases involved in the initial steps of the hemoglobin degradation pathway, a critical stage in the *Plasmodium falciparum* life cycle during human infection. Thus, they are attractive targets for novel therapeutic compounds to treat malaria, which remains one of the world's biggest health

problems. The three-dimensional structures available for *P. falciparum* plasmepsins II and IV make structure-based drug design of antimalarial compounds that focus on inhibiting plasmepsins possible. However, the structural flexibility of the plasmepsin active site cavity combined with insufficient knowledge of the functional residues and of those determining the specificity of parasitic enzymes is a drawback when designing specific inhibitors. In this study, we have combined a sequence and structural analysis with molecular dynamics simulations to predict the functional residues in *P. falciparum* plasmepsins. The careful analysis of X-ray structures and 3D models carried out here suggests that residues Y17, V105, T108, L191, L242, Q275, and T298 are important for plasmepsin function. These seven amino acids are conserved across the malarial strains but not in human aspartic proteases. Residues V105 and T108 are localized in a flap of an interior pocket and they only establish contacts with a specific non-peptide achiral inhibitor. We also observed a rapid conformational change in the L3 region of plasmepsins that closes the active site of the enzyme, which explains earlier experimental findings. These results shed light on the role of V105 and T108 residues in plasmepsin specificities, and they should be useful in structure-based design of novel, selective inhibitors that may serve as antimalarial drugs.

### Risk factors associated with uncontrolled hypertension: findings from the baseline CARMEN survey in Cienfuegos, Cuba.

Ordúñez P, Barcelo A, Bernal JL, Espinosa A, Silva LC, Cooper R. *J Hypertens*. 2008 Apr;26(4):663-671.

**Objectives** Identifying methods to improve pharmacologic control of elevated blood pressure remains the most urgent challenge in clinical research on hypertension. The probability of having inadequate control varies widely in the population and better understanding of the factors responsible could help to focus treatment strategies. **Methods** A population-based community survey of 1,475 persons aged 25–74 years, in Cienfuegos, Cuba, was used to identify these factors in a low-resource setting. **Results** While half of women with hypertension were controlled, only one-third of men were receiving successful treatment. Gender differences were not seen, however, among those currently taking medications. The largest burden of hypertension in absolute terms was concentrated in the age range 45–64, emphasizing the heavy burden of uncontrolled high blood pressure that falls on middle-aged men. Race-ethnicity was not a determinant of treatment and control status, nor was inability to obtain medication. **Conclusions** These findings largely confirm the pattern observed in industrialized countries and demonstrate the near-universal challenge confronting primary-care systems in physician-based control of cardiovascular risk factors. 