

## 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](http://www.medicc.org/mediccreview).

**Abdominal pain and asthenia as common clinical features in hospitalized children for giardiasis.** Almira P, Núñez FA, Bello J, González OM, Fernández R, Escobedo AA. *Acta Trop.* 2013 May 18. pii: S0001-706X(13)00131-9. doi: 10.1016/j.actatropica.2013.05.005. [Epub ahead of print]

Giardiasis is a disease with worldwide distribution, although its prevalence differs from country to country. In order to investigate the clinical pattern of giardiasis in in-patient children, a case-control study was carried out. In-patient children who had *Giardia lamblia* infection were compared with non *Giardia*-infected children, focusing only on 4 clinical manifestations: diarrhea, abdominal pain, asthenia and vomiting. In multivariable analysis, abdominal pain (odds ratio [OR] 4.71, 95% confidence intervals [CI] 2.66-8.32) and asthenia (OR 3.30, 95% CI 1.16-9.37) had positive and independent associations with *Giardia* infection. The present study supports the potential role of *G. lamblia* in abdominal pain in children who attend- and are admitted- to a hospital in Havana City, and highlights the importance to keep abdominal pain and asthenia in mind in hospital admitted children in the event of an association with an evocative epidemiological context.

**Antitumor effects of electrochemical treatment.** Camué Ciria HM, Morales González M, Ortiz Zamora L, Bergues Cabrales LE, Sierra González GV, de Oliveira LO, et al. *Chin J Cancer Res.* 2013 Apr;25(2):223–34.

Electrochemical treatment is an alternative modality for tumor treatment based on the application of a low intensity direct electric current to the tumor tissue through two or more platinum electrodes placed within the tumor zone or in the surrounding areas. This treatment is noted for its great effectiveness, minimal invasiveness and local effect. Several studies have been conducted worldwide to evaluate the antitumoral effect of this therapy. In all these studies a variety of biochemical and physiological responses of tumors to the applied treatment have been obtained. By this reason, researchers have suggested various mechanisms to explain how direct electric current destroys tumor cells. Although, it is generally accepted this treatment induces electrolysis, electro osmosis and electroporation in tumoral tissues. However, action mechanism of this alternative modality on the tumor tissue is not well understood. Although the principle of electrochemical treatment is simple, a standardized method is not yet available. The mechanism by which electrochemical treatment affects tumor growth and survival may

represent more complex process. The present work analyzes the latest and most important research done on the electrochemical treatment of tumors. We conclude with our point of view about the destruction mechanism features of this alternative therapy. Also, we suggest some mechanisms and strategies from the thermodynamic point of view for this therapy. In the area of electrochemical treatment of cancer this tool has been exploited very little and much work remains to be done. Electrochemical treatment constitutes a good therapeutic option for patients that have failed the conventional oncology methods.

**Combined meningococcal serogroup A and W135 outer-membrane vesicles activate cell-mediated immunity and long-term memory responses against non-covalent capsular polysaccharide A.** Romeu B, Lastre M, García L, Cedré B, Mandariote A, Fariñas M, et al. *Immunol Res.* 2013 May 10. [Epub ahead of print]

Outer-membrane vesicles (OMVs) have inherent adjuvant properties, and many vaccines use OMV as vaccine components. Utilizing the adjuvant properties of OMV could lead to the formulation of vaccines that are less expensive and potentially more immunogenic than covalently conjugated polysaccharide vaccines. We evaluated the adjuvant effect in Balb/c mice of combinations of OMV from *Neisseria meningitidis* serogroup A and W135 as compared to that of the non-covalently conjugated capsular polysaccharide A. Both antigens were adsorbed onto aluminum hydroxide. The mice were given a booster dose of plain polysaccharide A to stimulate an immunologic memory response. Subclasses determination and cytokine assays demonstrated the capacity of OMV to induce a IgG2a/IgG2b isotype profile and IFN- $\gamma$  production, suggesting the induction of a Th1 pattern immune response. Lymph proliferative responses to OMVs were high, with affinity maturation of antibodies observed. Bactericidal titers after the booster dose were also observed. Memory B cells and long-term memory T cells were also detected. The results of this study indicate that combined meningococcal serogroup A and W135 OMV can activate cell-mediated immunity and induce a long-term memory response.

**Couples at risk for spinocerebellar ataxia type 2: the Cuban prenatal diagnosis experience.** Cruz-Mariño T, Velázquez-Pérez L, González-Zaldivar Y, Aguilera-Rodríguez R, Velázquez-Santos M, Vázquez-Mojena Y, et al. *J Community Genet.* 2013 May 15. [Epub ahead of print]

Cuba reports the highest worldwide prevalence of spinocerebellar ataxia type 2 (SCA2) and the greatest number of descendants at risk. A protocol for genetic counseling, presymptomatic testing, and prenatal diagnosis of hereditary ataxias has been under development since 2001. Considering that the revision of the experience with prenatal diagnosis for SCA2 in Cuba would enable comparison of ours with international findings, we designed a descriptive study, based on the retrospective revision of the medical records belonging to the 58 couples that requested their inclusion in the program, during an 11-year period (2001-2011). Most of the participants in the prenatal diagnosis program were known presymptomatic carriers, diagnosed through the presymptomatic testing in the same period of study, for an uptake among them of 22.87 % (51 out of 223). In 28 cases, the fetuses were carriers, 20 of these couples (71.43 %) decided to terminate the pregnancy; the rest continued the pregnancy to term, this resulting in a predictive test for their unborn children. A predominance of females as the at-risk progenitor was observed. Except for a slightly lower average age, the results attained in the Cuban SCA2 prenatal diagnosis program resulted similar to the ones reported for Huntington disease in other countries. It is necessary to have easy access to the Cuban program through its expansion to other genetic centers along the island. Future research is needed to evaluate the long-term impact of both the predictive testing in unborn children and the selection of other reproductive options by the at-risk couples.

**Cuban Adolescents Requesting Presymptomatic Testing for Spinocerebellar Ataxia Type 2.** Cruz Velázquez L, González Y, Aguilera R, Velázquez M, Vázquez Y. *Genetics.* 2013 Apr. doi:10.54022013837202.

Since 2001 a program for the presymptomatic testing of families affected with SCA2 has been under development in Cuba. According to the initial protocol, access would be given to non-symptomatic individuals at 50% risk, over 18 years; nevertheless, eleven minors requested their inclusion in the program. A retrospective and descriptive study based on the analysis of the medical records belonging to these individuals was designed. Being aware of how challenging clinical settings of predictive genetic testing for minors are, this paper reviews their profile, the outcome of the carried out studies, as well as the reproductive option chosen by the gene positive consultants. The mean age at the time of testing was 16.2 years. Nine adolescents completed the protocol (three had positive test results) and two withdrew. They had a distinctive

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profile; all were females, pregnant, motivated by the risk assessment for their descendants, and interested in PND with termination of the gestation were the fetus a carrier. Nevertheless, once the result of the test is known, the gene positive consultants chose discordant reproductive options. Further research is necessary to assess the long-term psychological impact in both gene positive and gene negative participants, as well as in their parents and at-risk relatives.

**Deworming is not a risk factor for the development of atopic diseases: a longitudinal study in Cuban school children.** Van der Werf SD, Twisk JWR, Wordemann M, Campos Ponce M, Junco Díaz R, Núñez FA, et al. *Clin Experim Allergy*. 2013 Jun;43(6):665–71.

**Background** Soil-transmitted helminth (STH) infections have been suggested to protect from allergic sensitization and atopic diseases. Consequently, anthelmintic treatment would increase the prevalence of atopic disease in STH endemic populations. **Objective** To investigate the effect of deworming on allergic sensitization and atopic diseases in Cuban schoolchildren. **Methods** We followed up 108 STH positive schoolchildren aged 5–13 in six-monthly intervals for 24 months. Four consecutive groups of, respectively, 104, 56, 68, and 53 STH positive children were used as 'untreated' reference groups to assess general time trends. STH infections were diagnosed by stool examination. Asthma, allergic rhinoconjunctivitis, and atopic dermatitis were diagnosed by International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire and allergic sensitization by skin prick testing (SPT). At each time point, STH positive children were treated with one single dose of 500 mg mebendazole. **Results** After deworming, the frequency of asthma significantly decreased ( $P < 0.001$ ) while the frequency of allergic rhinoconjunctivitis and atopic dermatitis was not affected ( $P = 0.129$  and  $P = 0.751$ , respectively). The percentage of SPT positives temporarily increased ( $P < 0.001$ ) and subsequently returned to nearly baseline values ( $P = 0.093$ ). In the reference groups, no change over time was observed in the proportion of children with allergic sensitization and atopic diseases ( $P > 0.05$ ). **Conclusion & Clinical Relevance** Our results indicate that atopic diseases do not increase after anthelmintic treatment. Allergic sensitization on the other hand increases after deworming. As this increase appears only temporarily, deworming of schoolchildren does not seem to be a risk factor for the development of allergic sensitization, nor for atopic diseases.

**Effectiveness of a multidimensional approach for the prevention of ventilator-associated pneumonia in an adult intensive care unit in Cuba: Findings of the International Nosocomial Infection Control Consortium (INICC).** Guanache-Garcell H, Morales-Pérez C, Rosenthal VD. *J Infect Public Health*. 2013 Apr;6(2):98–107. doi: 10.1016/j.jiph.2012.11.009. Epub 2013 Feb 13.

**Objective** This study sought to assess the effect of the multidimensional approach developed by the International Nosocomial Infection Control Consortium (INICC) on the reduction of ventilator-associated pneumonia (VAP) rates in patients hospitalized in an adult intensive care unit (AICU) in an INICC member hospital in Havana, Cuba. **Methods** We conducted a prospective surveillance pre-post study in AICU patients. The study was divided into two periods: baseline and intervention. During the baseline period, we conducted active prospective surveillance of VAP using the Centers for Disease Control and Prevention (CDC) National Health Safety Network (NHSN) definition and INICC methods. During the intervention period, we implemented the INICC multidimensional approach for VAP, in addition to performing active surveillance. This multidimensional approach included the following measures: a bundle of infection control interventions, education, outcome surveillance, process surveillance, feedback of VAP rates and performance feedback of infection control practices. The baseline rates of VAP were compared to the rates obtained after intervention, and we analyzed the impact of our interventions by Poisson regression. **Results** During the baseline period, we recorded 114 mechanical ventilator (MV) days, whereas we recorded 2350MV days during the intervention period. The baseline rate of VAP was 52.63 per 1000MV days and 15.32 per 1000MV days during the intervention. At the end of the study period, we achieved a 70% reduction in the rate of VAP (RR, 0.3; 95% CI, 0.12–0.7;  $P$  value, 0.003.). **Conclusions** The implementation of the INICC multidimensional approach for VAP was associated with a significant reduction in the VAP rate in the participating AICU of Cuba.

**Evaluation of enteric-coated tablets as a whole cell inactivated vaccine candidate against *Vibrio cholerae*.** Fernández S, Año G, Castaño J, Pino Y, Uribarri E, Riverón LA, et al. *Travel Med Infect Dis*. 2013 Mar 8. pii: S1477-8939(13)00012-4. doi: 10.1016/j.tmaid.2012.10.006. [Epub ahead of print]

A vaccine candidate against cholera was developed in the form of oral tablets to avoid difficulties during application exhibited by current whole cell inactivated cholera vaccines. In this study, enteric-coated tablets were used to improve the protection of the active compound from gastric acidity. Tablets containing heat-killed whole cells of *Vibrio cholerae* strain C7258 as the active pharmaceutical compound was enteric-coated with the polymer Kollicoat® MAE-100P, which protected them efficiently from acidity when a disintegration test was carried out. Enzyme-linked immunosorbent assay (ELISA) anti-lipopolysaccharide (LPS) inhibition test and Western blot assay revealed the presence of *V. cholerae* antigens as LPS, mannose-sensitive haemagglutinin (MSHA) and outer membrane protein U (Omp U) in enteric-coated tablets. Immunogenicity studies (ELISA and vibriocidal test) carried out by intraduodenal

administration in rabbits showed that the coating process of tablets did not affect the immunogenicity of *V. cholerae*-inactivated cells. In addition, no differences were observed in the immune response elicited by enteric-coated or uncoated tablets, particularly because the animal model and immunization route used did not allow discriminating between acute resistances of both tablets formulations in vivo. Clinical studies with volunteers will be required to elucidate this aspect, but the results suggest the possibility of using enteric-coated tablets as a final pharmaceutical product for a cholera vaccine.

**Health and economic implications of first-line antiretroviral treatment of HIV/AIDS: Cuba 2001–2010.** Collazo Herrera M, Sánchez Valdés L, Tápanez Peraza R, Martínez Rodríguez A, Sosa Lorenzo I. *Intl J Care Pathw*. 2013 Apr 9.

The purpose of this study was to conduct an assessment of the economic and health impacts of global access on antiretroviral therapy (ARV) with the first-line national generic drugs for HIV/AIDS during 10 years of widespread use in Cuba. We used the technique of budget impact analysis to estimate the economic benefit by potentially avoiding costs in import substitution, based on the therapeutic equivalence demonstrated by bioequivalence studies conducted on generic drugs regarding patented medicine and to evaluate scenarios, using simple linear regression analysis to assess the existence of a decrease in the morbidity and mortality of AIDS cases. The use of ARV treatment with national generic drug resulted in a decrease of the morbidity and mortality of patients, and cost avoided could potentially be USD \$ 46 million, savings more than 60% of the annual health budget for purchase of these patented products. In conclusion, ARV therapy with national generic drug has demonstrated the political will of the Cuban government to solve the problem of accessibility of treatment to patients and to obtain therapeutic benefit, at a more reasonable cost to the country and more efficiency compared with patented drugs.

**High Clonal Diversity in a Non-Outbreak Situation of Clinical ESBL-Producing *Klebsiella pneumoniae* Isolates in the First National Surveillance Program in Cuba.** Quiñones D, Valverde A, Rodríguez-Baños M, Kobayashi N, Zayaz A, Abreu M, et al. *Microb Drug Resist*. 2013 May 21. [Epub ahead of print]

This work summarized the results obtained in an institutional *Klebsiella pneumoniae* surveillance program recently implemented in Cuba. Eighteen hospitals from five regions provided a total of 228 *K. pneumoniae* isolates (164 from admitted patients, four from hospital environmental sources, and 60 isolates from community patients). The genetic relationship was assessed by pulsed-field gel electrophoresis and multilocus sequence typing. Antimicrobial susceptibility was determined by the agar

dilution method, and blaESBL genes were sequenced. Fifty four *K. pneumoniae* isolates were extended-spectrum  $\beta$ -lactamases (ESBL)-producers (23.6%), mostly due to the CTX-M-15 enzyme (79.6%). ESBL isolates were grouped in 27 different sequence types (STs), being the most prevalent ST15 (15%), ST152 (13%), and both ST48 and ST147 (11%, respectively). Community-acquired criteria could be demonstrated in 60 patients (26%) corresponding to urological (33%), wound (27%), respiratory (27%), and otic (13%) infections. Population structure analysis showed that our isolates corresponded to a highly polyclonal population with 10 nonpreviously described STs, demonstrating the importance of local epidemiological studies. We report the first data of the population structure of ESBL-producing *K. pneumoniae* isolates obtained in a national multicenter surveillance Cuban program. Results showed that a highly polyclonal ESBL-producer *K. pneumoniae* population was mainly due to CTX-M-15 carriage, whereas carbapenemases production was not present.

**Immunosenescence and gender: a study in healthy Cubans.** García Verdecia B, Saavedra Hernández D, Lorenzo Luaces P, Badía Alvarez TD, Leonard Rupalé I, Mazorra Herrera Z, et al. *Immun Ageing*. 2013 Apr 30;10(1):16.

**Background** The progressive decline in the immune function during ageing is termed immunosenescence. Previous studies have reported differences between males and females in the distribution and cell responses of lymphocyte subsets. Most studies of immunosenescence have been done in populations of industrialized countries living in a rather cold environment, and facing lower antigenic challenges such as Cytomegalovirus (CMV). The aim of this study was to determine the effect of ageing on lymphocytes in a population with a high prevalence of CMV infection in all ages, and to compare gender differences related to the immunosenescence markers. **Results** Different populations of peripheral blood leukocytes from healthy young and old IgG-CMV seropositive individuals were examined using flow cytometry. With age, the number and frequency of B cells and T cells significantly decreased, while highly differentiated T cells increased. Such changes were different in males and females. The age-associated decline of less differentiated lymphocyte subsets (CD19, CD4 and CD8 cells) and the increase of highly differentiated T cells were more prominent in females. In males, there were no significant changes in CD19, CD4 and CD8 subsets but there was a significant increase in the proportion of highly differentiated T cells. **Conclusions** Shifts in lymphocyte subsets distribution were influenced by age and gender in an IgG-CMV seropositive population. These results suggest different patterns of immunosenescence in respect to gender differences. These patterns could have implications in the design of immunotherapy in the elderly.

**Is there any room for therapeutic vaccination against the HIV-1/AIDS?** Iglesias E. *Hum Vaccin Immunother*. 2013 Apr 9;9(7). [Epub ahead of print]

Any therapeutic vaccination approach against HIV-1 must induce CTL and Th1 cells. But, therapeutic vaccination is more than that. For extensive application of a therapeutic vaccine several questions need to be solved in advance to achieve a global impact. In this commentary some of them are addressed. We analyze the epidemiology, sociology, economy and immunopathology related to the HIV/AIDS disease. Also, important technical issues and real possibilities to overcome at least some of the major limitation of the antiretroviral treatments in the pursuit of an effective vaccine are considered. From the integration of previous analyses some conclusions are drawn. Because it is just a commentary some arguments are not unveiled into their full extension. At the end, we discuss some issues in relation to the development of the vaccine candidate TERA-VAC-HIV-1 as a case study.

**Medical treatments for incomplete miscarriage.** Neilson JP, Gyte GM, Hickey M, Vázquez JC, Dou L. *Cochrane Database Syst Rev*. 2013 Mar 28;3:CD007223.

**Background** Miscarriage occurs in 10% to 15% of pregnancies. The traditional treatment, after miscarriage, has been to perform surgery to remove any remaining placental tissues in the uterus ('evacuation of uterus'). However, medical treatments, or expectant care (no treatment), may also be effective, safe and acceptable. **Objectives** To assess the effectiveness, safety and acceptability of any medical treatment for incomplete miscarriage (before 24 weeks). **Search Methods** We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (30 November 2012) and reference lists of retrieved papers. Selection Criteria Randomised controlled trials comparing medical treatment with expectant care or surgery or alternative methods of medical treatment. Quasi-randomised trials were excluded. **Data Collection and Analysis** Two review authors independently assessed the studies for inclusion, assessed risk of bias and carried out data extraction. Data entry was checked. **Main Results** Twenty studies (4208 women) were included. There were no trials specifically of miscarriage treatment after 13 weeks' gestation. Three trials involving 335 women compared misoprostol treatment (all vaginally administered) with expectant care. There was no statistically significant difference in complete miscarriage (average risk ratio (RR) 1.23, 95% confidence interval (CI) 0.72 to 2.10; two studies, 150 women, random-effects), or in the need for surgical evacuation (average RR 0.62, 95% CI 0.17 to 2.26; two studies, 308 women, random-effects). There were few data on 'deaths or serious complications'. Twelve studies involving 2894 women addressed the comparison of misoprostol (six studies used oral administration, four studies used vaginal,

one study sub-lingual, one study combined vaginal + oral) with surgical evacuation. There was a slightly lower incidence of complete miscarriage with misoprostol (average RR 0.97, 95% CI 0.95 to 0.99, 11 studies, 2493 women, random-effects) but with success rate high for both methods. Overall, there were fewer surgical evacuations with misoprostol (average RR 0.06, 95% CI 0.02 to 0.13; 11 studies, 2654 women, random-effects) but more unplanned procedures (average RR 5.82, 95% CI 2.93 to 11.56; nine studies, 2274 women, random-effects). There were few data on 'deaths or serious complications'. Nausea was more common with misoprostol (average RR 2.41, 95% CI 1.44 to 4.03; nine studies, 2179 women, random-effects). Five trials compared different routes of administration and/or doses of misoprostol. There was no clear evidence of one regimen being superior to another. Limited evidence suggests that women generally seem satisfied with their care. Long-term follow-up from one included study identified no difference in subsequent fertility between the three approaches. **Authors conclusions** The available evidence suggests that medical treatment, with misoprostol, and expectant care are both acceptable alternatives to routine surgical evacuation given the availability of health service resources to support all three approaches. Women experiencing miscarriage at less than 13 weeks should be offered an informed choice. Future studies should include long-term follow-up.

**Molecular and phylogenetic analysis of influenza A H1N1 pandemic viruses in Cuba, May 2009 to August 2010.** Ramos AP, Herrera BA, Ramírez OV, García AA, Jiménez MM, Valdés CS, et al. *Int J Infect Dis*. 2013 Feb 24. pii: S1201-9712(13)00080-5. doi: 10.1016/j.ijid.2013.01.028. [Epub ahead of print]

The influenza A(H1N1)pdm09 virus was detected in Cuba in May 2009. The introduction of a new virus with increased transmissibility into a population makes surveillance of the pandemic strain to the molecular level necessary. The aim of the present study was the molecular and phylogenetic analysis of pandemic influenza A(H1N1)pdm09 strains that circulated in Cuba between May 2009 and August 2010. Seventy clinical samples were included in the study. Nucleotide sequences from the hemagglutinin HA1 region segment were obtained directly from clinical samples. Genetic distances were calculated using MEGA v.5.05. A phylogenetic tree was constructed using MrBayes v.3.1.2 software. Potential N-glycosylation sites were predicted using NetNGlyc server 1.0. The 48 Cuban sequences of influenza A(H1N1)pdm09 obtained were similar to the A/California/07/2009 (H1N1) vaccine strain. Most of the Cuban strains belonged to clade 7. Cuban viruses showed amino acid changes, some of them located at three antigenic sites: Ca, Sa, and Sb. Two dominant mutations were detected: P83S (100%) and S203T (85.7%). Glycosylation site analysis revealed the gain of one site at position 162 in 13 sequences. The findings in this study

contribute to our understanding of the progress of the influenza A(H1N1)pdm09 virus, since this virus is at the starting point of its evolution in humans.

**Phylogenetic Analysis of Human T Cell Lymphotropic Virus Type 1 Isolated from Cuban Individuals.** Machado LY, Navea LM, Díaz HM, Blanco M, Dubed M, Romay DM, et al. *AIDS Res Hum Retroviruses*. 2013 May 15. [Epub ahead of print]

The presence of infection by human T cell lymphotropic virus type 1 (HTLV-1) in Cuba has been previously documented. However, genetic information on the strains that circulate in the Cuban people remains unknown. The present work constitutes the first study of phylogenetic relationship of HTLV-1 Cuban isolates. Twelve Cuban patients who were diagnosed with HTLV-1 infection and had different clinical manifestations were studied. The 3' LTR sequences were analyzed for the construction of a phylogenetic tree with reference sequences of HTLV-1 of different geographic origins. Phylogenetic analysis of the 3' LTR gene showed that all the Cuban samples clustered in the Transcontinental subgroup of the Cosmopolitan subtype. Phylogenetic analysis suggests multiple introductions of HTLV-1 in Cuba as well as a possible African origin of the samples. The results of the study will reinforce the program of epidemic surveillance of the infection in Cuba.

**Population-wide weight loss and regain in relation to diabetes burden and cardiovascular mortality in Cuba 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends.** Franco M, Bilal U, Orduñez P, Benet M, Morejón A, Caballero B, et al. *BMJ*. 2013 Apr 9;346:f1515. doi: 10.1136/bmj.f1515.

**Objective** To evaluate the associations between population-wide loss and gain in weight with diabetes prevalence, incidence, and mortality, as well as cardiovascular and cancer mortality trends, in Cuba over a 30 year interval. **Design** Repeated cross sectional surveys and ecological comparison of secular trends. **Setting** Cuba and the province of Cienfuegos, from 1980 to 2010. **Participants** Measurements in Cienfuegos included a representative sample of 1657, 1351, 1667, and 1492 adults in 1991, 1995, 2001, and 2010, respectively. National surveys included a representative sample of 14 304, 22 851, and 8031 participants in 1995, 2001, and 2010, respectively. **Main Outcome Measures** Changes in smoking, daily energy intake, physical activity, and body weight were tracked from 1980 to 2010 using national and regional surveys. Data for diabetes prevalence and incidence were obtained from national population based registries. Mortality trends were modelled using national vital statistics. **Results** Rapid declines in diabetes and heart disease accompanied an average population-wide loss of 5.5 kg in weight, driven by an economic cri-

sis in the mid-1990s. A rebound in population weight followed in 1995 (33.5% prevalence of overweight and obesity) and exceeded pre-crisis levels by 2010 (52.9% prevalence). The population-wide increase in weight was immediately followed by a 116% increase in diabetes prevalence and 140% increase in diabetes incidence. Six years into the weight rebound phase, diabetes mortality increased by 49% (from 9.3 deaths per 10 000 people in 2002 to 13.9 deaths per 10 000 people in 2010). A deceleration in the rate of decline in mortality from coronary heart disease was also observed. **Conclusions** In relation to the Cuban experience in 1980-2010, there is an association at the population level between weight reduction and death from diabetes and cardiovascular disease; the opposite effect on the diabetes and cardiovascular burden was seen on population-wide weight gain.

**Reference values of the bioimpedance vector components in a Caribbean population.** Nescolarde L, Núñez A, Bogóñez P, Lara A, Vailiant G, Morales R, et al. *e-SPEN J*. 2013 Jun 10.

**Background & aims** Application of bioelectrical impedance vector analysis (BIVA) requires comparison of an impedance vector to reference intervals derived from healthy subjects. The aim of this work is to obtain reference nomograms of bioimpedance vectors from healthy subjects living in Santiago de Cuba. **Methods** A sample of 4030 healthy people, ages 2–80 y, was measured using a tetra-polar whole-body bioimpedance analyzer at 50 kHz. BIVA method uses the 50, 75 and 95% confidence ellipses of reference populations to classify individual and group vectors. **Results** The 95% confidence ellipses derived among boys and girls (2–12 y) were similar ( $P > 0.05$ ) with significant gender differences ( $P < 0.05$ ) throughout adulthood. Furthermore, we can observe a progressive decrease in the modulus of the impedance with age with the same phase angle from 13 to 59 y. However, in both genders on subjects  $>60$  y we also observed a phase downfall, possibly due to the reduction of mass and structure, by sarcopenia. **Conclusions** Reference ellipses are provided, distributed in six sets resulting in age separation intervals (not in gender) for children from 2 to 12 y; two gender specific reference ellipses for teenagers in the range of 13–16 y, for adults from 17 to 59 y and for elderly people from 60 to 80 y.

**Risk factors for wheezing in infants born on Cuba.** Venero SJ, Suárez R, Mora EC, García G, del Valle I, Gómez L, et al. *QJM*. 2013 Jul 3. [Epub ahead of print].

**Background** Cuba is a unique country, and despite limited economic development has an excellent health system. However, the prevalence of asthma symptoms in children in Havana, Cuba, is unusually high. **Aim** Since early life exposures are critical to the aetiology of asthma, we have studied environmental influences on the risk of wheeze in Cuban

infants. **Design** Cross-sectional study. **Methods** A random sample of 2032 children aged 12-15 months living in Havana was selected for inclusion in the cohort. Data were collected using questionnaires administered by researchers. **Results** Of 2032 infants invited to participate, 1956 (96%) infants provided data. The prevalence of any wheeze was 45%, severe wheeze requiring use of the emergency services was 30%, and recurrent wheeze on three or more occasions was 20%. The largest adjusted risk factors for any wheeze were presence of eczema (odds ratio OR 2.09; 95% confidence intervals 95% CI: 1.48-2.94), family history of asthma (OR 2.05; 95% CI: 1.60-2.62), poor ventilation in the home (OR 1.99; 95% CI: 1.48-2.67), attendance at nursery (OR 1.78; 95%CI: 1.24-2.57), male sex (OR1.52; 95% CI: 1.19-1.96) and the number of smokers in the house ( $p < 0.03$  for trend), OR 1.64 (95%CI: 1.17-2.31) for three or more smokers in home compared to no smokers in the household. **Conclusion** We have identified several risk factors for any wheeze in young infants living in modern day Cuba. As the prevalence of smoking in the home is high (51%), intervention studies are required to determine effective strategies to improve infant health.

**Safety of the production process of SURFACEN® to inactivate and remove virus.** Sánchez Y, Noa E, Alfonso W, Dubed M, Alvarez G, Navea L, et al. *Biologicals*. 2013 May 9. pii: S1045-1056(13)00036-5. doi: 10.1016/j.biologicals.2013.04.003. [Epub ahead of print]

SURFACEN® is a biological product produced from pig lungs. Since these animals can be potential sources of microbial pathogens such as viruses, the manufacturing process of this product should guarantee safety from health hazards. The SURFACEN® production procedure is capable of effective viral clearance (inactivation/removal) by involving two stages of organic solvent extraction followed by acetone precipitation and heat treatment. In this study, we evaluated the clearance capacity of these four stages for a wide range of viruses by performing spiking experiments. Residual contamination was assessed using a Tissue Culture Infectious Dose assay (log<sub>10</sub> TCID<sub>50</sub>). The validation study demonstrated that, for all viruses tested, the TCID<sub>50</sub> titers were reduced by more than 2 log<sub>10</sub> in each stage. Total log reduction values achieved were between  $\geq 17.82$  log<sub>10</sub> and  $\geq 27.93$  log<sub>10</sub>, depending on the virus physical properties, titer, and the number of processing stages applied. Results indicated that the production procedure of SURFACEN® can inactivate or remove contaminant viruses from the raw material.

**Secondary infection as a risk factor for dengue hemorrhagic fever/dengue shock syndrome: a historical perspective and role of antibody-dependent enhancement of infection.** Guzman MG, Alvarez M, Halstead SB. *Arch Virol*. 2013 Mar 8. [Epub ahead of print]

Today, dengue viruses are the most prevalent arthropod-borne viruses in the world. Since the 1960s, numerous reports have identified a second heterologous dengue virus (DENV) infection as a principal risk factor for severe dengue disease (dengue hemorrhagic fever/dengue shock syndrome, DHF/DSS). Modifiers of dengue disease response include the specific sequence of two DENV infections, the interval between infections, and contributions from the human host, such as age, ethnicity, chronic illnesses and genetic background. Antibody-dependent enhancement (ADE) of dengue virus infection has been proposed as the early mechanism underlying DHF/DSS. Dengue cross-reactive antibodies raised following a first dengue infection combine with a second infecting virus to form infectious immune complexes that enter Fc-receptor-bearing cells. This results in an increased number of infected cells and increased viral output per cell. At the late illness stage, high levels of cytokines, possibly the result of T cell elimination of infected cells, result in vascular permeability, leading to shock and death. This review is focused on the etiological role of secondary infections (SI) and mechanisms of ADE.

**Spatial Distribution and Contamination Assessment of Heavy Metals in Urban Topsoils from Las Tunas City, Cuba.** Díaz Rizo O, Fonticiella Morell D, Arado López JO, Borrell Muñoz JL, D'Alessandro K, López Pino N. Bull Environ Contam Toxicol. 2013 Jul;91(1):29–35.

Concentrations of Cr, Co, Ni, Cu, Zn, Pb and Fe in the topsoils (0-10 cm) from Las Tunas city were measured by X-ray fluorescence analysis. The mean Cr, Co, Ni, Cu, Zn and Pb contents in the urban topsoil samples ( $97 \pm 30$ ,  $14 \pm 2$ ,  $35 \pm 36$ ,  $94 \pm 26$ ,  $199 \pm 87$  and  $42 \pm 29$  mg kg<sup>-1</sup> dry weight, respectively) were compared with mean concentrations for other cities around the world with similar population. Cr content in school grounds, parks and residential areas exceed in 20 % the average Cr background level. Highest content for Ni was determined in residential areas, for Zn in market gardens soils and as for Pb, the highest topsoil-background content ratios were observed for market gardens (2.7) and residential areas (2.3). Spatial distribution maps indicated the same behaviour for Cr-Co-Ni and Pb-Zn, respectively, whereas the spatial distribution of Cu differs from other heavy metals. On the other hand, the metal-to-iron normalisation, using (10-20 cm) bottom soil contents as background, showed that topsoils in Las Tunas city are severely enriched with lead and not enriched with the rest of the determined metals. The average values of integrated pollution index (IPI) indicated that soils are moderately contaminated by heavy metals ( $1.17 \leq \text{IPI}_{\text{ave}} \leq 1.39$ ), but enrichment index values shows that metal concentrations on the studied locations are not above the permissible levels for urban agriculture.

**The Cuban Program for Predictive Testing of SCA2: 11 Years and 768 Individuals to**

**Learn From.** Cruz Mariño T, Velázquez Pérez L, González Zaldivar Y, Aguilera Rodríguez R, Velázquez Santos M, Vázquez Mojena Y, et al. Clin Genet. 2013 Mar 15. doi: 10.1111/cge.12142. [Epub ahead of print]

Having reported the world's highest prevalence of SCA2, health professionals in Cuba developed a program for the predictive testing of this condition. Between February 2001 and December 2011 a total of 1050 individuals requested their inclusion in the presymptomatic testing program. Their medical records were retrospectively analyzed in the present descriptive study. A total of 768 participants completed the protocol, 204 withdrew and 78 were excluded. The presymptomatic testing uptake was 24.91%. Females predominated and 70.96% had negative test results. Their main motivations were risk assessment in their descendants, physical and psychological preparation to cope with the disease and planning for the future. The profile of Cuban participants in the predictive testing program is similar to the one reported for other programs all over the world, nevertheless the genetic counseling practice at the community level is a distinctive aspect, which is valuable in providing at-risk individuals with wide and proper knowledge before their testing inclusion request. The SCA2 predictive testing program has high uptake rates and is renowned in our population. Future research is needed to assess the long-term psychological impact in the participants, their partners and relatives. 