

Cuban Research in Current International Journals

A bibliometric study of international scientific productivity in giardiasis covering the period 1971-2010. Escobedo AA, Arencibia R, Vega RL, Rodríguez-Morales AJ, Almirall P, Alfonso M. *J Infect Dev Ctries.* 2015 Jan 15;9(1):76–86.

Introduction Despite years of relative neglect, interest in *Giardia* infection seems to be recently growing, perhaps in part due to its inclusion into the World Health Organization's Neglected Diseases Initiative since 2004. The purpose of this study was to provide an overview of *Giardia* and giardiasis research over time, as represented by the quantity of published papers. **Methodology** Data for this study were collected from the electronic PubMed/Medline database of National Library of Medicine's (NLM), due to its easy accessibility and wide use. It was accessed online between April and December 2011. Data for the period 1971-2010 were obtained and information was downloaded using the EndNote program developed by Thomson Reuters. **Results** During the study period, a total of 6,964 references (articles, reviews, editorials, letter to the editor, etc.) covering different aspects of *Giardia* and giardiasis were located in the PubMed database after applying the search strategy reported above. Most papers were original articles and published in English. **Conclusions** In this first effort to explore the development and research productivity on giardiasis over time (no previously published bibliometric studies on giardiasis exist), two interesting characteristics of the *Giardia* and giardiasis literature were discovered: the concentration of papers over journals disseminating the research results, and that research in this field is growing and will likely continue to grow in the coming years.

A systems approach to resilience in the built environment: the case of Cuba. Lizarralde G, Valladares A, Olivera A, Bornstein L, Gould K, Barenstein JD. *Disasters.* 2015 Jan;39 Suppl 1:S76–95.

Through its capacity to evoke systemic adaptation before and after disasters, resilience has become a seductive theory in disaster management. Several studies have linked the concept with systems theory; however, they have been mostly based on theoretical models with limited empirical support. The study of the Cuban model of resilience sheds light on the variables that create systemic resilience in the built environment and its relations with the social and natural environments. Cuba is vulnerable to many types of hazard, yet the country's disaster management benefits from institutional, health and education systems that develop social capital, knowledge and other assets that support construction industry and housing development, systematic urban and regional planning, effective alerts, and evacuation plans. The Cuban political context is specific, but the study can nonetheless contribute to systemic improvements to the resilience of built environments in other contexts.

Attentional selection of levels within hierarchically organized figures is mediated by object-files. Valdés-Sosa MJ, Iglesias Fuster J, Torres R. *Front Integr Neurosci.* 2014 Dec 16;8:91. DOI: 10.3389/fnint.2014.00091. eCollection 2014.

Objects frequently have a hierarchical organization (tree-branch-leaf). How do we select the level to be attended? This has been explored with compound letters: a global letter built from local letters. One explanation, backed by much empirical support, is that attentional competition is biased toward certain spatial frequency (SF) bands across all locations and objects (a SF filter). This view assumes that the global and local letters are carried respectively by low and high SF bands, and that the bias can persist over time. Here we advocate a complementary view in which perception of hierarchical level is determined by how we represent letters in object-files. Although many properties bound to an object-file (i.e., position, color, even shape) can mutate without affecting its persistence over time, we posit that same object-file cannot be used to store information from different hierarchical levels. Thus, selection of level would be independent from locations but not from the way objects are represented at each moment. These views were contrasted via an attentional blink paradigm that presented letters within compound figures, but only one level at a time. Attending to two letters in rapid succession was easier if they were at the same-compared to different-levels, as predicted by both accounts. However, only the object-file account was able to explain why it was easier to report two targets on the same moving object compared to the same targets on distinct objects. The interference of different masks on target recognition was also easier to predict by the object-file account than by an SF filter. The methods introduced here allowed us to investigate attention to hierarchical levels and to object-files within the same empirical framework. The data suggests that SF information is used to structure the internal organization of object representations, a process understood best by integrating object-file theory with previous models of hierarchical perception.

Cardiac outcomes 3 years after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: value of myocardial perfusion imaging and coronary calcium score Peix A, Cabrera LO, Rodríguez L, Padrón K, Llanes J, Licea M, et al. *Nucl Med Commun.* 2015 Feb;36(2):156–61.

Objective The aim of the study was to identify the possible association among myocardial perfusion imaging (MPI) variables, coronary calcium score (CCS), and adverse events at medium term in type 2 asymptomatic diabetes mellitus patients. **Materials and methods** Patients who participated in a first study that included a stress-rest MPI and a CCS assessment were asked to take part in this study. The present study protocol required a control single-photon emission computerized tomography after 3 years. Forty-one patients gave their informed consent. **Results** Of the 41 patients, 13 (32%) showed perfusion defects at the initial MPI. Of them, at 3 years, five continued showing perfusion defects, whereas another two had new defects (incidence of ischemia of 17%). Thus, 61% of the initial positive MPIs were normal at 3 years ($P=0.04$). In these cases the therapy was modified between the two studies. Left ventricular ejection fraction at stress showed a slight increase at 3 years ($P=NS$). Ventricular volumes significantly decreased at 3 years ($P < 0.01$). Three patients (7.3%) developed an event during the follow-up (FU): two noncardiac deaths and one non-ST elevation myocardial infarction. The only variables that showed a possible association with the occurrence of events at FU were a CCS higher than 100 and less than 5 metabolic equivalents (METS) reached during the stress test ($P=0.01$). **Conclusion** A CCS higher than 100 and a low functional capacity (< 5 METS), but not an abnormal MPI, can be associated with cardiac events at 3-year FU in asymptomatic type 2 diabetic patients.

Detection of anti-streptococcal, antienolase, and anti-neural antibodies in subjects with early-onset psychiatric disorders. Nicolini H, López Y, Genis-Mendoza AD, Manrique V, López-Canovas L, Niubo E, et al. *Actas Esp Psiquiatr.* 2015 Mar;43(2):35–41.

Introduction Infection with group A Streptococcus (StrepA) can cause post-infectious sequelae, including a spectrum of childhood-onset obsessive-compulsive (OCD) and tic disorders with autoimmune origin (PANDAS, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections). Until now, no single immunological test has been designed that unequivocally diagnoses these disorders. In this study, we assessed the detection of serum antibodies against human brain enolase (AE), neural tissue (AN) and Streptococcus (AS) as a laboratory tool for the diagnosis of early-onset psychiatric disorders. **Methodology** Serum antibodies against human brain enolase, total brain proteins, and total proteins from StrepA were detected by ELISA in 37 patients with a presumptive diagnosis of PANDAS and in 12 healthy subjects from Mexico and Cuba. **Results** The antibody titers against human brain enolase (AE) and Streptococcal proteins (AS) were higher in patients than in control subjects (t -student, $t_{AE}=-2.17$, $P=0.035$; $t_{AS}=-2.68$, $P=0.01$, $n=12$ and 37 /group, $df=47$, significance level 0.05), while the neural antibody titers did not differ between the two groups ($P(t)=0.05$). The number of subjects (titers $>$ meancontrol + CI_{95}) with simultaneous seropositivity to all three antibodies was higher in the patient group (51.4%) than in the control group (8.3%) group ($X^2=5.27$, $P=0.022$, $df=1$, $n=49$). **Conclusions** The simultaneous detection of all three of these antibodies could provide valuable information for the etiologic diagnosis of individuals with early-onset obsessive compulsive disorders associated with streptococcal infection and, consequently, for prescribing suitable therapy.

HBV genotypic variability in Cuba. Loureiro CL, Aguilar JC, Aguilar J, Muzio V, Pentón E, García D, et al. *PLoS One.* 2015 Mar 5;10(3): e0118959. doi: 10.1371/journal.pone.0118959.

The genetic diversity of HBV in human population is often a reflection of its genetic admixture. The aim of this study was to explore the genotypic diversity of HBV in Cuba. The S genomic region of Cuban HBV isolates was sequenced and for selected isolates the complete genome or precore-core sequence was analyzed. The most frequent genotype was A (167/250, 67%), mainly A2 (149, 60%) but also A1 and one A4. A total of 77 isolates were classified as genotype D (31%), with co-circulation of several subgenotypes (56 D4, 2 D1, 5 D2, 7 D3/6 and 7 D7). Three isolates belonged to genotype E, two to H and one to B3. Complete genome sequence analysis of selected isolates confirmed the phylogenetic analysis performed with the S region. Mutations or polymorphisms in precore region were more common among genotype D compared to genotype A isolates. The HBV genotypic distribution in this Caribbean island correlates with the Y lineage genetic background of the population, where a European and African origin prevails. HBV genotypes E, B3 and H isolates might represent more recent introductions.

Hospital based multicenter study in Spain, Mexico and Cuba on attitudes to living liver donation. A Ríos, López-Navas AI, Ayala-García MA, Sebastián MJ, Abdo-Cuza A, Martínez-Alarcón L, et al. *Gastroenterol Hepatol.* 2015 Jan 23. DOI: 10.1016/j.gastrohep.2014.12.004. [Epub ahead of print]. Spanish.

Introduction Given the lack of a sufficient number of livers available for transplantation, living liver donation (LLD) is being developed in the Spanish-speaking world. To do this, it is essential that health workers in hospitals are in favor of such donation, given that they are a key component in this treatment and that their attitudes influence public opinion. **Objective** To analyze attitude toward LLD among hospital personnel from healthcare centers in Spain and Latin America. **Materials and methods** Ten hospitals were selected from the «International Donor Collaborative Project»: 3 from Spain, 5 from Mexico and 2 from Cuba. Random sampling stratified by type of service and job category was used. Attitudes to LLD were evaluated through a validated questionnaire on psychosocial aspects. The questionnaire was anonymous and self-administered. Statistical tests consisted of Student's T test, the chi-square test and logistic regression analysis. **Results** Of the 2,618 employees surveyed, 85% (n=2,231) were in favor of related LLD; of these, 31% (n=804) were in favor of unrelated LLD. No association was found between the country of the interviewed, personal-social variables or work-related variables. The following factors were associated with a favorable attitude toward related LLD donation: having had personal experience of donation and transplantation ($P < .001$); being in favor of deceased donation ($P < .001$); believing that one might need a possible transplant ($P < .001$); being in favor of living kidney donation ($P < .001$); being willing to accept a liver from a living donor ($P < .001$); having discussed the matter of donation and transplantation within the family ($P < .001$) and with one's partner ($P < .001$); carrying out pro-social type activities ($P < .001$); being Catholic ($P = .040$); believing that one's religion is in favor of donation and transplantation ($P < .001$); and not being concerned about the possible mutilation of the body after donation ($P < .001$). **Conclusion** Hospital personnel from Spain and Latin America had a favorable attitude toward LLD, which was associated with factors directly and indirectly related to donation and transplantation, family and religious factors, and attitudes toward the body.

Immune network, the dangerous liaisons in pain: a short review. León-Toirac EJ. *J Pain Relief.* 2015 Jan;4:1.

Introduction Pain has increasingly become an important health problem. However, few doctors at primary health care are qualified to treat it. Recent researches also suggest that neurons are not the only ones involved in the establishment and maintenance of pain. This short review was conceived to collect some information on the contribution of immune system to the pathogenesis of pain and also to shed light to other mechanisms connected to this process. **Development** Inflammation at the damaged site generates a cascade of events that produce innate immune cells concentration and activation; as well as production of pro-inflammatory cytokines, hormonal factors and neurotropic activators of glial cells, which in turn perturb synaptic transmission. This entire complex induces pain persistence. **Concluding remarks** The recognized commitment of immune, endocrine and nervous cells in pathological changes related with pain is crucial to offer new and satisfactory approaches to solve this problem. Integral modulation of these agents would contribute to new effective alternatives in the handling of pain.

Incidence of dementia and association with APOE genotype in older Cubans. Llibre Rodríguez JJ, Valhuerdi Cepero A, Sánchez Gil IY, López Medina AM, Llibre Guerra JC, Llibre Guerra JJ, et al. *Dement Neuropsychol.* 2014 Dec;8(4):356–63.

Objective In an admixed population of older Cubans, the incidence and association of APOE and sociodemographic risk factors with dementia incidence was estimated. **Methods** A single-phase survey (baseline) of over 65-year-olds residing in seven catchment areas in Cuba (n=2944) was conducted between 2003 and 2007. Dementia diagnosis was established according to DSM-IV and 10/66 criteria. APOE genotype was determined in 2520 participants. An incidence wave was conducted 4.5 years after cohort inception in order to estimate incidence and associations with sociodemographic risk factors of the APOE $\epsilon 4$ genotype. **Results** The incidence rate of DSM IV dementia was 9.0 per 1000 person-years (95% CI 7.2-11.3) and of 10/66 dementia were 20.5 per 1000 person-years (95% CI, 17.6-23.5). Older age, a family history of dementia and APOE $\epsilon 4$ genotype were independent risk factors for incident 10/66 dementia. APOE genotype was associated cross-sectionally with dementia prevalence, but the effect on the incidence of dementia was attenuated, and only apparent among those in the youngest age group. **Conclusion** The incidence of dementia in the older Cuban population is relatively high and similar to levels reported in Europe and North-America. The study showed that the relationship between APOE $\epsilon 4$ and incident dementia is stronger in the younger-old than the older-old and that this change must be taken into account in models of dementia.

Influence of the quality of infrastructure in the development of medical technologies. Guerra RM, Meizoso MC, Ramírez JR. In: Braidor A, Hadad A, editors. Proceedings of the 6th Latin American Congress on Biomedical Engineering CLAIB. Vol. 49; 2014 Oct 29–31; Paraná, Argentina. Paraná: IFMBE; 2015. p. 746–49.

The national quality infrastructure is the result of the integration and coordination of several interrelated subjects: metrology, standardization, testing, accreditation, and certification. In this paper the impact of such infrastructure on the field of Cuban medical technologies and its present role as a technical tool for regulators are analyzed. The use of specific standards for medical technologies within the framework of risk and quality management systems, based on reliable measurements, is the basic infrastructure to guarantee the efficacy and minimize the risks of medical devices commercialized in the Cuban National Health System. Nevertheless, not all these elements are well established in the country. So, for the further development of the medical device sector a strengthening of the national quality infrastructure is indispensable.

Insecticide resistance and metabolic mechanisms involved in larval and adult stages of *Aedes aegypti* insecticide-resistant reference strains from Cuba. Bisset JA, Rodríguez MM, French L, Severson DW, Gutiérrez G, Hurtado D, et al. J Am Mosquito Control Assoc. 2014 Dec;30(4):298–304.

Studies were conducted to compare levels of insecticide resistance and to determine the metabolic resistance mechanisms in larval and adult stages of *Aedes aegypti* from Cuba. Three insecticide-resistant reference strains of *Ae. aegypti* from Cuba were examined. These strains were derived from a Santiago de Cuba strain isolated in 1997; it was previously subjected to a strong selection for resistance to temephos (SAN-F6), deltamethrin (SAN-F12), and propoxur (SAN-F13) and routinely maintained in the laboratory under selection pressure up to the present time, when the study was carried out. In addition, an insecticide-susceptible strain was used for comparison. The insecticide resistance in larvae and adults was determined using standard World Health Organization methodologies. Insecticide resistance mechanisms were determined by biochemical assays. The esterases (α EST and β EST) and mixed function oxidase (MFO) activities were significantly higher in adults than in the larvae of the three resistant strains studied. The association of resistance level with the biochemical mechanism for each insecticide was established for each stage. The observed differences between larval and adult stages of *Ae. aegypti* in their levels of insecticide resistance and the biochemical mechanisms involved should be included as part of monitoring and surveillance activities in *Ae. aegypti* vector control programs.

Lymphoscintigraphy for the assessment of autologous stem cell implantation in chronic lymphedema. Peña Quián Y, Hernández Ramírez P, Batista Cuéllar JF, Perera Pintado A, Coca Pérez MA. Clin Nucl Med. 2015 Mar;40(3):217–9.

Lymphoscintigraphy is the criterion standard technique for the diagnosis of lymphedema. The authors present the images acquired before and 6 months after implantation of autologous stem cells in 2 patients with chronic lymphedema of the lower limbs. The stem cells implantations were carried out by multiple superficial and deep injections in the trajectory of the lymphatic vessels and also in the inguinal region. A volume of 0.75 to 1.00 mL of cell suspension ($1.0\text{--}2.2 \times 10^9$ stem cells) was administered in each injection site. The anatomy and function of the lymphatic system were evaluated.

Masculinities in Cuba: description and analysis of a case study from a gender perspective. Formental Hernández S, Hernández Pita I, Fernández de Juan T. MCS. 2014 Oct;(3):220–47.

This study aims to deepen our discussion about Cuban men's current perception about hegemonic masculinity, based on an extensive literary review and a survey focusing on 125 males who attend a Mental Health Center in Havana. Using gender as a concept and category to unravel the relations between sexual difference and inequality, the authors present the results of their descriptive and transversal research, designed to address multiple cases, from a qualitative methodological perspective (QMP method) and compare them with other findings, especially from Latin America. The research techniques applied, expose how the patriarchal culture continues imposing a burden on the minds of many Cuban men, while they also exhibit the rise of a new generation which enjoys a less genitalist sexuality, willing to sharing their new outlook and beginning to manifest a liberating and positive distance from machismo.

Mifepristone 5 mg versus 10 mg for emergency contraception: double-blind randomized clinical trial Carbonell JL, García R, González A, Breto A, Sánchez C. *Int J Womens Health*. 2015 Jan 12;7:95–102. DOI: 10.2147/IJWH.S65793. eCollection 2015.

Purpose To estimate the efficacy and safety of 5 mg and 10 mg mifepristone for emergency contraception up to 144 hours after unprotected coitus. **Methods** This double-blind randomized clinical trial was carried out at Eusebio Hernandez Hospital (Havana, Cuba). A total of 2,418 women who requested emergency contraception after unprotected coitus received either 5 mg or 10 mg mifepristone. The variables for assessing efficacy were the pregnancies that occurred and the fraction of pregnancies that were prevented. Other variables assessed were the side effects of mifepristone, vaginal bleeding, and changes in the date of the following menstruation. **Results** There were 15/1,206 (1.2%) and 9/1,212 (0.7%) pregnancies in the 5 mg and 10 mg group, respectively ($P=0.107$). There were 88% and 93% prevented pregnancies in the 5 mg and un ≥ 7 days was experienced by 4.9% and 11.0% of subjects in the 5 mg and 10 mg group, respectively ($P=0.001$). There was a significant high failure rate for women weighing >75 kg in the 5 mg group. **Conclusion** It would be advisable to use the 10 mg dose of mifepristone for emergency contraception as there was a trend suggesting that the failure rate of the larger dose was lower.

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Multimodal imaging in nonlesional medically intractable focal epilepsy Morales-Chacón LM, Sánchez Catusus AC, Báez Martín M, Rodríguez Rojas R, Lorigados Pedre L, Estupiñán Díaz B. *Front Biosci (Elite Ed)*. 2015 Jan 1;7:48–65.

Identification and localization of epileptogenic zone (EZ) is vital in patients with medically-intractable focal epilepsy, who may be candidates for potentially curative resective epilepsy surgery. Presence of a lesion on magnetic resonance imaging (MRI) influences both diagnostic classification and selection for surgery. However, the implications for MRI-negative cases are not well-defined for such patients. Most of these patients undergo invasive long-term Electroencephalography recordings before a final decision regarding resection is possible. Recent developments in structural and functional neuroimaging which include quali-quantitative MRI, Positron Emission Tomography, Single Photon Emission Computed Tomography, and functional MRI have significantly changed presurgical epilepsy evaluation. Source analysis based on electrophysiological information, using either EEG or magnetoencephalography are also promising in order to noninvasively localize the EZ and to guide surgery in medically-intractable focal epilepsy patients that exhibit nonlesional MRI. This chapter aims to review the value of the combined use of structural and functional imaging techniques, and how this multimodal approach improves both selection of surgical candidates and post-operative outcomes in medically-intractable nonlesional focal epilepsy.

No effect of insecticide treated curtain deployment on Aedes infestation in a cluster randomized trial in setting of low dengue transmission in Guantanamo, Cuba Toledo ME, Vanlerberghe V, Lambert I, Montada D, Baly A, Van der Stuyft P. *PLoS One*. 2015 Mar 20;10(3) e0119373. DOI: 10.1371/journal.pone.0119373.

Objective & methodology The current study evaluated the effectiveness and cost-effectiveness of Insecticide Treated Curtain (ITC) deployment for reducing dengue vector infestation levels in the Cuban context with intensive routine control activities. A cluster randomized controlled trial took place in Guantanamo city, east

Cuba. Twelve neighborhoods (about 500 households each) were selected among the ones with the highest *Aedes* infestation levels in the previous two years, and were randomly allocated to the intervention and control arms. Long lasting ITC (PermaNet) was distributed in the intervention clusters in March 2009. Routine control activities were continued in the whole study area. In both study arms, we monitored monthly pre- and post-intervention House Index (HI, number of houses with at least 1 container with *Aedes* immature stages/100 houses inspected), during 12 and 18 months respectively. We evaluated the effect of ITC deployment on HI by fitting a generalized linear regression model with a negative binomial link function to these data. **Principal findings** At distribution, the ITC coverage (% of households using ≥ 1 ITC) reached 98.4%, with a median of 3 ITC distributed/household. After 18 months, the coverage remained 97.4%. The local *Aedes* species was susceptible to deltamethrin (mosquito mortality rate of 99.7%) and the residual deltamethrin activity in the ITC was within acceptable levels (mosquito mortality rate of 73.1%) after one year of curtain use. Over the 18 month observation period after ITC distribution, the adjusted HI rate ratio, intervention versus control clusters, was 1.15 (95% CI 0.57 to 2.34). The annualized cost per household of ITC implementation was 3.8 USD, against 16.8 USD for all routine ACP activities. **Conclusions** Deployment of ITC in a setting with already intensive routine *Aedes* control actions does not lead to reductions in *Aedes* infestation levels.

Overlap and diversity in antimicrobial peptide databases: compiling a non-redundant set of sequences Aguilera-Mendoza L, Marrero-Ponce Y, Tellez-Ibarra R, Llorente-Quesada MT, Salgado J, Barigye SJ, et al. *Bioinformatics*. 2015 Mar 29. pii: btv180. [Epub ahead of print]

Motivation The large variety of antimicrobial peptide databases developed to date is characterized by a substantial overlap of data and similarity of sequences. Our goals are to analyze the levels of redundancy for all available antimicrobial peptide databases and use this information to build a new non-redundant sequence database. For this purpose, a new software tool is introduced. **Results** A comparative study of 25 antimicrobial peptide databases reveals the overlap and diversity among them and the internal diversity within each database. The overlap analysis shows that only one database (Peptaibol) contains exclusive data, not present in any other, while all sequences in the LAMP Patent database are included in CAMP Patent. However, the majority of databases have their own set of unique sequences, as well as some overlap with other databases. The complete set of non-duplicate sequences comprises 16990 cases, which is almost half of the total number of reported peptides. On the other hand, the diversity analysis identifies the most and least diverse databases and proves that all databases exhibit some level of redundancy. Finally, we present a new parallel free software, named Dover Analyzer, developed to compute the overlap and diversity between any number of databases and compiling a set of non-redundant sequences. These results are useful for selecting or building a suitable representative set of antimicrobial peptides, according to specific needs. **Availability** The regularly updated non-redundant sequence databases and the Dover Analyzer software to perform custom analysis are available at <http://mobiosd-hub.com/doveranalyzer/> CONTACT: ymarrero77@yahoo.es.

Performance of an in-house human immunodeficiency virus type 1 genotyping system for assessment of drug resistance in Cuba Alemán Y, Vinken L, Kourí V, Pérez L, Álvarez A, Abrahantes Y, et al. *PLoS One*. 2015 Feb 11;10(2): e0117176. DOI: 10.1371/journal.pone.0117176.

As commercial human immunodeficiency virus type 1 drug resistance assays are expensive, they are not commonly used in resource-limited settings. Hence, a more affordable in-house procedure was set up taking into account the specific epidemiological and economic circumstances of Cuba. The performance characteristics of the in-house assay were evaluated using clinical samples with various subtypes and resistance patterns. The lower limit of amplification was determined on dilutions series of 20 clinical isolates and ranged from 84 to 529 RNA copies/mL. For the assessment of trueness, 14 clinical samples were analyzed and the ViroSeq HIV-1 Genotyping System v2.0 was used as the reference standard. The mean nucleotide sequence identity between the two assays was $98.7\% \pm 1.0$. Additionally, 99.0% of the amino acids at drug resistance positions were identical. The sensitivity and specificity in detecting drug resistance mutations was respectively 94.1% and 99.5%. Only few discordances in drug resistance interpretation patterns were observed. The repeatability and reproducibility were evaluated using 10 clinical samples with 3 replicates per sample. The in-house test was very precise as nucleotide sequence identity among paired nucleotide sequences ranged from 98.7% to 99.9%. The acceptance criteria were met by the in-house test for all performance characteristics, demonstrating a high degree of accuracy. Subsequently, the applicability in routine clinical practice was evaluated on 380 plasma samples. The amplification success rate was 91% and good quality consensus sequences encoding the entire protease and the first 335 codons in reverse transcriptase could be obtained for 99% of the successful amplicons. The reagent cost per sample using the in-house procedure was around € 80 per genotyping attempt. Overall, the in-house assay provided good

results, was feasible with equipment and reagents available in Cuba and was half as expensive as commercial assays.

Protective effect of a lipid-based preparation from mycobacterium smegmatis in a Murine Model of Progressive Pulmonary Tuberculosis García MA, Borrero R, Lanio ME, Tirado Y, Alvarez N, Puig A, et al. *Biomed Res Int.* 2014 Dec 7. DOI:10.1155/2014/273129

A more effective vaccine against tuberculosis (TB) is urgently needed. Based on its high genetic homology with *Mycobacterium tuberculosis* (Mtb), the nonpathogenic mycobacteria, *Mycobacterium smegmatis* (Ms), could be an attractive source of potential antigens to be included in such a vaccine. We evaluated the capability of lipid-based preparations obtained from Ms to provide a protective response in Balb/c mice after challenge with Mtb H37Rv strain. The intratracheal model of progressive pulmonary TB was used to assess the level of protection in terms of bacterial load as well as the pathological changes in the lungs of immunized Balb/c mice following challenge with Mtb. Mice immunized with the lipid-based preparation from Ms either adjuvanted with Alum (LMs-AL) or nonadjuvanted (LMs) showed significant reductions in bacterial load ($P < 0.01$) compared to the negative control group (animals immunized with phosphate buffered saline (PBS)). Both lipid formulations showed the same level of protection as Bacille Calmette and Guerin (BCG). Regarding the pathologic changes in the lungs, mice immunized with both lipid formulations showed less pneumonic area when compared with the PBS group ($P < 0.01$) and showed similar results compared with the BCG group. These findings suggest the potential of LMs as a promising vaccine candidate against TB.

Psychometric properties of EURO-D, a geriatric depression scale: a cross-cultural validation study Guerra M, Ferri C, Llibre J, Prina AM, Prince M. *BMC Psychiatry.* 2015 Feb;15(1):12.

Background Many of the assessment tools used to study depression among older people are adaptations of instruments developed in other cultural setting. There is a need to validate those instruments in low and middle income countries (LMIC). **Methods** A one-phase cross-sectional survey of people aged [greater than or equal to] 65 years from LMIC. EURO-D was checked for psychometric properties. Calibration with clinical diagnosis was made using ICD-10. Optimal cutpoint was determined. Concurrent validity was assessed measuring correlations with WHODAS 2.0. **Results** 17,852 interviews were completed in 13 sites from nine countries. EURO-D constituted a hierarchical scale in most sites. The most commonly endorsed symptom in Latin American sites was depression; in China was sleep disturbance and tearfulness; in India, irritability and fatigue and in Nigeria loss of enjoyment. Two factor structure (affective and motivation) were demonstrated. Measurement invariance was demonstrated among Latin American and Indian sites being less evident in China and Nigeria. At the 4/5 cutpoint, sensitivity for ICD-10 depressive episode was 86% or higher in all sites and specificity exceeded 84% in all Latin America and Chinese sites. Concurrent validity was supported, at least for Latin American and Indian sites. **Conclusions** There is evidence for the cross-cultural validity of the EURO-D scale at Latin American and Indian settings and its potential applicability in comparative epidemiological studies.

Residual vasomotor activity assessed by heart rate variability in a brain-dead case Machado C, Estévez M, Pérez-Nellar J, Schiavi A. *BMJ Case Rep.* 2015 Apr 1. DOI: 10.1136/bcr-2014-205677.

Background A patient assessed by heart rate variability (HRV) methodology, beginning just after the completion of brain death (BD) diagnosis, showed remaining very low frequency (VLF) waves for approximately 10 min. A time-varying spectral analysis showed that during the first 550 s, a significant power spectral density remained in the high-frequency (HF), low-frequency (LF) and VLF bands. From 550 to 675 s, the HF oscillations totally vanished, and a marked progressive decay of the LF and VLF power density occurred. After 700 s the VLF undulations stopped and remaining small amplitude oscillations at 0.2 Hz coincided with the ventilator frequency. The VLF oscillations recorded in our case might be related to residual sympathetic vasomotor activity that progressively disappeared due to the extension of necrosis affecting the nervous centers of the lower part of the medulla and the first 2-3 cervical spine segments.

Semi-mechanistic model to characterize non-linear pharmacokinetic of nimotuzumab in patients with advanced breast cancer Rodríguez-Vera L, Suzarte MR, Fernández-Sánchez E, Soriano JL, Peraire Guitart C, Castañeda-Hernández G, et al. *J Clin Pharmacol.* 2015 Mar 11. DOI: 10.1002/jcph.496. [Epub ahead of print]

This study aims i) to develop a semi-mechanistic pharmacokinetic (PK) model for nimotuzumab, in patients with advanced breast cancer ii) to identify demographic, biochemical and clinical predictive factors of the PK

variability. Data from a phase I study were analyzed using the nonlinear mixed effects approach (NONMEM). A target-mediated disposition model that included two-open PK compartments, the mAb-target binding and target and mAb-target complex turnovers, described best the linear and non-linear PK. Covariates had no influence on the PK parameters. The final parameter estimates were 19.93 L (steady state volume), 0.0045 L/h-0.0172 L/h (total clearance values range), 6.96 µg/mL (steady state binding constant), 5.50 h⁻¹ (target degradation rate constant), 1.43 (µg/mL) • h⁻¹ (complex formation rate), 0.148 h⁻¹ (complex internalization rate constant). The model described the effect of the mAb-target binding, and target and mAb-target complex turnovers on nimotuzumab PK. Simulations showed that doses above 200 mg maintained the 50% target occupancy during all the treatment. This model can be very useful to know the dosing schedules required for efficacy and supports further investigation on the pharmacokinetic/pharmacodynamic relationships of nimotuzumab in order to improve its therapeutic use.

Serum zinc levels of cord blood: relation to birth weight and gestational period Gómez T, Bequer L, Mollineda A, González O, Díaz M, Fernández D. *J Trace Elem Med Biol.* 2015 Jan 5. DOI: 10.1016/j.jtemb.2014.12.009. [Epub ahead of print]

Background Zn-deficiency has been associated with numerous alterations during pregnancy including low birth weight; however, the research relating neonatal zinc status and birth weight has not produced reliable results. **Objective** To compare the serum Zn-levels of cord blood in healthy newborns and low birth weight newborns, and to assess a possible relationship between zinc concentration and neonatal birth weight and gestational age. **Materials and methods** 123 newborns divided in "study group" (n=50) with < 2500g birth weight neonates and "control group" (n=73) with ≥2500g birth weight neonates were enrolled. Study group was subdivided according to gestational age in preterm (< 37 weeks) and full-term (≥37 weeks). Serum cord blood samples were collected and the Zn-levels were analyzed using flame Atomic Absorption Spectrophotometry method and the result was expressed in µmol/L. The Zn-levels were compared between the groups (Mann-Whitney-U test) and the Zn-levels were correlated with the birth weight and gestational age (Spearman's rank correlations). **Results** Statistically significant low positive correlation between Zn-levels and birth weight (p=0.283; p=0.005) was found. No statistically significant difference between Zn-levels of study and control groups [17.00±0.43 vs. 18.16±0.32 (p=0.053)] was found. Statistically significant low positive correlation between Zn-levels and gestational age (p=0.351; p=0.001) was found. No statistically significant difference between Zn-levels of preterm as compare to full-term newborns [16.33±0.42 vs. 18.43±0.93 (p=0.079)] was found. Zn-level of preterm subgroup was significantly lower compared to control group (p=0.001). **Conclusions** Despite low birth weight preterm neonates had significantly lower serum zinc levels of cord blood than healthy term neonates, the correlation between cord blood zinc levels and birth weight and gestational age was lower. The results are not enough to relate the change in cord blood zinc concentration to the birth weight values or gestational period. In relation to complicated pregnancies, further studies regarding zinc levels in blood in our population are required.

Torpid diabetic wound healing: evidence on the role of epigenetic forces Berlanga-Acosta J, Mendoza-Mari Y, Fernández-Mayola M, García-Ojalvo A, Valdés-Pérez C, Savigne-Gutiérrez W, et al. *Int J Diabetes Clin Res.* 2015 Jan 29;2(1).

The increasing number of diabetes patients represents a health challenge due to disease-related, end-organs complications. Hyperglycemia is considered the proximal trigger of an intricate cascade of molecular processes that progressively deteriorate tissues and organs, leading to the onset of clinical complications. Lower extremity ulcerations and their ensued refractoriness to heal can potentially result in amputation and disability and remain the second most feared diabetic complication. We have identified particular morphogenetic traits in diabetic foot ulcer granulation tissues and its cultured fibroblasts. Diabetic ulcer-derived fibroblasts conserve a sort of memory as their in vitro traits very much recapitulate the in vivo behavior, in terms of proliferative disabilities and transcriptional and post-translational modifications of genes involved in proliferation, migration and ECM dynamics. Furthermore, the acute, in vivo morphologic recreation of a microangiopathy in a neo-formed granulation tissue is worth mentioning. All these elements suggest that "metabolic memory," in which chromatin remodeling and long-lasting epigenetic changes play important roles, could contribute to the persistence of diabetic complications. Metabolic memory is largely responsible for the onset/perpetuation of the ulcers chronicity phenotype. The comprehensive understanding of the chromatin choreography underlying this pathogenic stream; and its potential pharmacologic manipulation would allow for future innovative therapies for diabetic complications, including wound healing refractoriness.