Tolerance and safety of benznidazol in adult patients with Chagas disease: experience in four public medical centers of Ciudad de Buenos Aires (CABA). Argentina

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Background: Chagas-Mazza disease, usually considered a neglected tropical diseases, is an important cause of morbidity and mortality in Latin America. Treatment in adult chronic asymptomatic patients is still in debate. Main limitations of traditional drugs are the adverse drug reactions (ADRs). Nevertheless treatment of young adults and women of childbearing age is proposed to be useful in decreasing progression to cardiovascular disease and mother to child transmission

Our objective is to evaluate tolerance and development of ADRs with benznidazol (BZN) in adult chronic asymptomatic patients with Chagas, in four public medical centers in CABA, a non-endemic area.

Methods & Materials: We conducted a descriptive-observational study of ADRs related to BZN treatment in four medical centers in CABA from 01/06/2012 to 01/10/2017. Patients between 18 and 65 years, without cardiovascular or digestive disease and Kushnir score of 0-1 were included. Pregnant or breastfeeding women, older than 65 years, or with Kushnir score 2-3 were excluded.

Included patients signed an informed consent, were advised on risks-benefits of the medication and prescribed recommendations to improve tolerance. BZN was used at 5mg/kg dose for 60 days. Daily self-monitoring records and weekly medical controls were performed. Telephone contacts were provided in case of eventualities.

Results: Eighty-seven adult patients, 20 male and 67 female, median age 39 (18-60) treated with BZD were included. Sixty-six (75.86%) completed treatment and 40 (45%) developed 67 episodes of ADRs. Only 5 episodes were severe. Most frequent reactions were gastrointestinal and cutaneous (80.6%) and only 1 was severe. Mild events represented 89.55% of the ADRs and could be managed with symptomatic treatment. Twenty one patients abandoned. Treatment interruption was indicated in only 6 patients. No mortality was observed.

ADRs are analyzed in Table 1

<table>
<thead>
<tr>
<th>Total ADRs</th>
<th>N</th>
<th>%</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>28</td>
<td>41.79%</td>
<td>28</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Rash</td>
<td>26</td>
<td>38.8%</td>
<td>23</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>5</td>
<td>7.46%</td>
<td>3</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Hematological</td>
<td>4</td>
<td>5.97%</td>
<td>2</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Neurological</td>
<td>4</td>
<td>5.97%</td>
<td>4</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusion: In our experience, BZN was safe in adults. Tolerance was acceptable and most of the adverse events were gastrointestinal and cutaneous, were mild and could be managed with symptomatic treatment with no mortality observed.
Is Haemophilus Influenzae type b (Hib) reemerging? 25 years of meningitis surveillance in a Pediatric Hospital in Buenos Aires metropolitan area


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Background: Hib was the main agent of acute bacterial meningitis in children under 5 years old in prevaccine era. In Argentina, routine vaccination began in 1998 (3 doses +1 booster schedule) resulting in a significant decline on Hib invasive disease rates. In the last years an increase in the national rates was observed. The aim of this study was to describe the epidemiological and clinical pattern of Hib meningitis (HibMen) comparing both pre and post vaccine periods.

Methods & Materials: All patients with confirmed HibMen admitted in "R. Gutierrez" Children's Hospital during 1992-2016 were included. Time-series analysis were performed comparing HibMen hospitalization rates between pre-vaccination (PreV) 1992-1997 and post-vaccination (PostV) 1999-2016 periods excluding intervention year (1998). PostV was subdivided in 3 equal periods (6 years each).

Results: A total of 85 patients with HibMen were included, 74% of them occurred in PreV; the largest number of cases in 1993 (19 cases). Median age was 9 months (5-15), 68% were males, 54% had complications (68% neurologic) and 22% had sequelae at discharge; no difference found between PreV and PostV; 7% had comorbidities. Lethality rate was 4.8% (4/83), all fatal cases in 1992-1998 periods. Vaccination reports of PostV cases (n=15): 10 (67%) incomplete primary series (4 delayed schedules) and 5 complete primary series (2 delayed schedules). Only one case had a booster dose. A significant overall reduction in HibMen hospitalization rate when comparing PreV vs PostV was -94.7% (CI95%: -89.8-97.3%; p<0.001) with differences among the three PostV periods (1999-2004:-98.5%; 2005-2010:-93.1%; 2011-2016:-80.9%.

Conclusion: HibMen cases were mostly healthy infants. A dramatic decrease of HibMen hospitalizations was observed after Hib vaccine introduction, but it seems to be reemerging in the last years. Booster vaccination coverage in almost all years was insufficient.
Evolution of gender-neutral HPV vaccination in National Immunization Calendars in Latin America and the Caribbean

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Background: In 2006 the US FDA approved the first Human Papillomavirus (HPV) vaccine for girls/women from 9 to 26 years of age. Since then many countries have licensed and adopted HPV vaccination for use in National Immunization Programs (NIP) for girls. In 2009 and 2010, the quadrivalent HPV vaccine was licensed for use in males from 9 to 26 years of age for prevention of genital warts and anal cancer, respectively. The ACIP recommended its routine vaccination for boys and girls in 2011.

Methods & Materials: The objective is to describe the evolution of the incorporation of Gender neutral vaccination (GNV) in NIP of Latin America and the Caribbean countries and territories (LAC) following initial introduction of female vaccination.

Comprehensive searches were conducted using official national government websites and complemented with the country profiles in the WHO immunization monitoring system.

Results: From a total of 44 countries and territories, 27 (61.3%) have HPV vaccine in their NIP. GNV programs have been adopted by eight countries, mostly via mixed strategy (school-based and health centers). The recommendation to include HPV immunization for males usually occurred several years after the initial introduction of female vaccination: Argentina (2011/2017), Barbados (2014/2016), Bermuda (2011/2016), Brazil (2014/2017), Panama (2008/2016), Puerto Rico (2007/2011) and Trinidad & Tobago (2013/2014). In 2017, Antigua introduced the HPV vaccine as GNV program. In the majority of the NIPs, the targeted age cohorts are the same for both genders, with the exception of Trinidad & Tobago which offers HPV vaccination from 11 -to 45 years of age for women and from 11 to 26 years of age for men. The addition of these GNV NIP programs means that approximately 9 million (~30%) of the total 28 million males, between 10-14 yo living in LAC, have access to vaccination through public programs.

Conclusion: Since 2016 an accelerated introduction of HPV vaccination programs targeting male populations has been observed. Around 32% of the 10-14 yo males, living in LAC, can potentially benefit from HPV vaccine. This reflects the increasing recognition of the importance of vaccinating males in order to achieve higher vaccination uptake and greater public health impact.
Effectiveness of boosted lopinavir versus boosted atazanavir in HIV-1 infected patients switching to second-line antiretroviral therapy following failure of an NNRTI first line ART in a low/middle-income setting, a retrospective cohort study: the BaLANCe study

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Background: Boosted protease inhibitor (PI) plus two nucleoside reverse transcriptase inhibitors (NRTI) is the preferred strategy for second-line anti-retroviral therapy (ART2) after the failure of a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based first-line (ART1). We aim at comparing lopinavir/ritonavir (LPV/r) and atazanavir plus ritonavir (ATV/r) ART2 in routine clinical practice in Buenos Aires.

Methods & Materials: Data were retrospectively collected from 3 clinical sites. Inclusion criteria: HIV+, ≥18 years; ART1 containing NNRTI + 2-3 N(t)RTIs; switched to ATV/r or LPV/r ART2 by treating physician due to virologic failure (2 pVL>400 or 1 pVL >1000 at least 180 days after ART2 initiation); ART1 from January-2007 and switch to ART2 before June-2015. Exclusion criteria: any use of ddl+TDF or ddl+d4T in ART2; other PIs, etravirine, maraviroc, enfuvirtide or integrase inhibitors previous or concomitant to ART2. Three outcomes were evaluated at week 48: ART2 discontinuation, virologic failure in those not discontinued and, treatment failure with discontinuations considered as failures. Predictors for each outcome were assessed through logistic regression.

Results: 162 patients were included: 93 patients (57%) received ATV/r based ART2 and 69 (43%) LPV/r. Patients on LPV/r were younger (36.0 vs. 39.2 years), had lower CD4 counts (179 vs. 229 cels/uL) and higher pVL (4.3 vs. 3.9 log copies/uL). Before week 48, 11 patients on ATV/r (11.8%) and 15 on LPV/r (21.7%) discontinued ART2, mainly due to gastrointestinal adverse events. Virologic failure in those not discontinued was similar for ATV/r and LPV/r (18% vs 22%). Treatment failure was observed in 24.7% and 36.2% respectively. After adjusting for sex, age and baseline pVL, LPV/r use was no longer associated with treatment failure (OR: 1.19, 95%CI: 0.52-2.73, p: 0.686) being pVL the main predictor (OR for pVL≥4 logs: 2.71, 95%CI: 1.16-6.32, p: 0.021)

Conclusion: In this retrospective cohort study of patients receiving ATV/r or LPV/r after failure of ART1, we found an increased risk of treatment discontinuation in LPV/r ART2 while virologic suppression in those on therapy was similar with both PIs. The main driver of virologic failure was pVL at start of ART2.
Aerobic etiology of intraabdominal infections in a public hospital. Surveillance and antibiotic resistance

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Background: The treatment of intraabdominal infections are empirically performed on the basis of existing epidemiological data. There are data in Argentine that present an increased resistance more than 30% to Ciprofloxacin and Ampicilin/sulbactam in E. coli and K. pneumoniae. The following study is performed in order to know the etiology and antimicrobial resistance in our region.

Methods & Materials: Retrospective, descriptive and observational study. The patients included not only had intraabdominal infection diagnosis but also any kind of surgery in order to control the source in the “Hospital Escuela de Agudos Dr. Ramón Madariaga” with positive aerobic bacteriological results between January 1st, 2016 and December 31st, 2016. Data were analyzed by the statistical support of IBM SPSS statistics v. 19.0. Epidemic registries were done. The analysis of bacteriological samples were developed in the “Laboratorio Nacional de Referencia del Instituto Carlos Malbrán (LNR)”.

Results: There were analyzed 69 intrabdominal infections, 59 acute appendicitis, male 45/69 (65.2%), middle aged 41 (15-86), comorbidities 23/69 (33%), previous use of antibiotics 10/69 (14.5%), previous hospital admission 4/69 (5.8%). The empirical treatment used was based on one drug with activity against aerobic pathogens in 68 cases (98.6%). The most frequent active drugs used were ciprofloxacin plus metronidazole 62/69 (89.9%) and ampicillin/sulbactam 4/69 (5.8%). 94 aerobic bacterias were isolated (1.4 bacterias/episodes), gram negative bacteria 82/94 (87.2%), Escherichia coli 55/94 (58.5%), Klebsiella pneumonia 10/94 (10.6%) and Pseudomonas aeruginosa 8/94 (8.5%). The resistance profile of the enterobacteria was ampicillin/sulbactam 27/69 (39%), ciprofloxacin 18/70 (26%), gentamicin 8/71 (11%), cefotaxime 4/71(6%) and piperacillin/tazobactam 3/71 (4%). In E. coli was ampicillin/sulbactam 23/55(42%), ciprofloxacin 15/55 (28%), gentamicin 6/53 (11%), amikacin 1/28 (4%), piperacillin/tazobactam 1/55 (2%) and cefotaxime 2/55(4%). In K. pneumoniae was ampicillin/sulbactam 3/10 (30%), ciprofloxacin 3/10 (30%), gentamicin 2/10(20%), piperacillin/tazobactam 2/10 (20%), cefotaxime 2/10 (20%), amikacin 0/5 (0%). There were no resistant in P. aeruginosa. Beta lactamase of extended spectrum 4/71.

Conclusion: The microbiological findings of this study provide information to base the election of antibiotic empirical treatments in our hospital. This findings lead us to ask the necessity of reconsider the antibiotics schemes empirically outlined to intrabdominal infection
Differences in the incidence of Carbapenem Resistant Enterobacteriae (CRE) and Vancomycin-resistant Enterococcus (VRE) in a major teaching hospital and factors with possible impact.

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**Background:** In the last year we have observed an increase in CRE in hospitalized patients but not in VRE inspite of discontinuation of isolation measures. Studies have associated CRE colonization with the changes in the microbiota (like Clostridium butyricum), caused by antibiotics.

**Methods & Materials:** Descriptive, retrospective.

<table>
<thead>
<tr>
<th>Results: Annual incidence of MDRO, first clinical sample &gt; 72 hours of admission, 1000 patient days.</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRE</td>
<td>0.41 (CI 95% 0.316; 0.518)</td>
<td>0.28 (CI 95% 0.207; 0.375)</td>
<td>0.22 (CI 95% 0.156; 0.3)</td>
<td>0.24 (CI 95% 0.17; 0.317)</td>
<td>0.48 (0.355; 0.634)</td>
</tr>
<tr>
<td>VRE</td>
<td>0.23 (CI 95% 0.16; 0.32)</td>
<td>0.04 (CI 95% 0.017; 0.09)</td>
<td>0.11 (CI 95% 0.06; 0.17)</td>
<td>0.18 (CI 95% 0.12; 0.25)</td>
<td>0.11 (0.0538; 0.192)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Factors</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand hygiene compliance (%)</td>
<td>62.8% (CI 95% 61.26; 64.4)</td>
<td>72.4% (CI 95% 71.07; 73.6)</td>
<td>65.5% (CI 95% 64.27; 66.77)</td>
<td>64.8% (CI 95% 63.8; 65.7)</td>
<td>74.1% (CI 95% 73; 75.26)</td>
</tr>
<tr>
<td>Broad spectrum antibiotic consumption, days of therapy, 1000 patient days (vancomycin, carbapenem, tigecycline, piperacillin-tazobactam and linezolid).</td>
<td>174.75 (95% CI 172.9; 176.6)</td>
<td>175.68 (173.8; 177.5)</td>
<td>190.23 (188.3; 192.1)</td>
<td>187.14 (181.2; 192.9)</td>
<td>193.16 (186.2; 200)</td>
</tr>
</tbody>
</table>

In 2016 contact precautions were discontinued for VRE and remained por CRE. Hand hygiene increases significantly in 2017 P 0.000. The antibiotics combined increase significantly from 2014 to 2015 RR 1.08 (95% CI 1.07; 1.1).

**Conclusion:** Comparing multidrug resistant organisms (MDRO) with gastrointestinal carriage, the rate of VRE remains stable and CRE continues to rise without an outbreak pattern. Antibiotic consumption is also on the rise. Despite the Antimicrobial Stewardship Programs, the same increase in the incidence of the MDRO promotes its use. Perhaps the time has come to consider also new tools such as probiotics and fecal microbiota therapy, focusing on the microbiota to resist colonization by CRE.
Target-Pathogen: A structural bioinformatic approach to prioritize drug targets in pathogens.

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Background: The successful use of antibiotics has been facing challenges because microbial pathogens are developing various forms of resistance. Despite this situation, new drug development projects have been inadequate for reasons ranging from bad selection of targets to reduced antimicrobial discovery efforts by pharmaceutical companies. Currently, it is accepted that identification of appropriate targets are critical steps for designing new drugs. In this sense, Next Generation Sequencing is increasingly aiding the evaluation of gene function, essentiality and suitability for drug development. Nevertheless there is a lack of online resources that allows genome wide based data consolidation define a list of potential targets. Here, we present Target-Pathogen (http://target.sbg.qb.fcen.uba.ar/patho) an online resource that facilitates the identification and prioritization of candidate targets suitable for new drug development.

Methods & Materials: Target Pathogen integrates omic data, focusing on essentiality, metabolic role and structural druggability prediction of proteins. Structural information of proteins was obtained from PDB or modelled using MODELLER. For or all the structures we compute several structural properties like: DrugScore, Active site residues or PFAM relevant residues. All proteins in the database were subjected to NCBI-BLASTp and to Database of Essential Genes to asses human homology and essentiability. Metabolic networks (MN) were built by using Pathway Tools and chokepoints and topological parameters were set.

Results: Target-Pathogen was designed to integrate and weigh protein information such as: function, metabolic role, off-targeting, structural properties including druggability, essentiality, and omic experiments, to facilitate the identification of candidate drug targets in pathogens. We include in the database ten genomes of some of the most relevant microorganisms for human health (Mycobacterium tuberculosis, Mycobacterium leprae, Klebsiella pneumoniae, Plasmodium vivax, Toxoplasma gondii, Leishmania major, Wolbachia bancrofti, Trypanosoma brucei, Shigella dysenteriae and Schistosoma Smanosoni) and show its applicability. New genomes can be uploaded upon request.

Conclusion: The goal of Target-Pathogen is not to replace wet strategies for target identification. Rather, our goal is to become a useful resource for researchers working in the field of target identification and/or drug discovery to translate biological questions in a computational tractable way by exploring, filtering and weighting the vast quantity of genome-scale data sets.
Febrile Neutropenia in Acute Myeloblastic Leukemia (AML) clinical and microbiological features of infectious episodes and evaluation of mortality.

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Background: An important life-threatening complication of chemotherapy administered in patients with acute myeloblastic leukemia is febrile neutropenia.

Objectives
Evaluate clinical, microbiological features and evolution of infectious episodes during neutropenia in patients with AML, and the variables associated with mortality.

Methods & Materials: Retrospective, descriptive study conducted in a private hospital of Buenos Aires City during the period January 2016-September 2017. Clinical records of patients with AML under chemotherapy were evaluated. We analyzed demographic, clinical data (absolute neutrophil count (ANC) at diagnosis of infectious episode, days of neutropenia, sites of infection, mortality) and microbiological data (microorganisms and antimicrobial resistance). Infectious episodes were classified in: 1-Microbiologically Documented (MD): a- Bacteremia of unknown origin (BUO) b- Bacteremia with site of infection (BSI) c- Infection clinically and microbiologically documented without bacteremia (MDCD) 2-Clinically documented (CD) 3-Possible infection (PI): no MD no CD.

Results: 134 infectious episodes were diagnosed during 39 episodes of neutropenia in 33 patients, mean age 58 (DS±18) years, female 78 (58%), mean duration of neutropenia 30 (DS±15) days, median ANC at diagnosis of infectious episode 41 cel/mm³ (range, 0-962). We found 3.2 (DS±1.7) infectious attacks by episode of neutropenia. Among the 134, MD 58 (43%): BUO 9 (7%), BSI 30 (22%), MDCD 19 (29%); CD 58 (43%) and PI 18 (13%). Most common sites of infection: Lung 33 (25%), intestinal tract 30 (22%), skin and mucosa 20 (15%); 39 bacteremias occurred with 43 isolations: gram negative (GN) 21 (49%), gram positive (GP) 18 (42%), fungemia 3 (7%), others 1 (2%). K pneumoniae was the most common GN and coagulase-negative staphylococci between GP. The prevalence of multi drug resistance microorganisms (MDRM) in bacteremia was: 8 (38%) in GN, and 6 (33%) in GP. Mortality rate was 12%. Duration of neutropenia, median ANC, site of infection, and isolation of MDRM were not associated with mortality. On univariate and multivariate analyses the variables found to be significantly associated with mortality were the presence of bacteremia (OR 8: IC 2,4-28; p=0.001) and age ≥60 years (OR 12: IC 2,56-61,7; p=0.002)

Conclusion: We found a high rate of bacteremia between infectious episodes, as well as high percentage of MDRM isolations. An age ≥60 years and the presence of bacteremia were associated with more probability of death.
Extensive diversity of SIVagm infecting synanthropic African green monkeys and Olive Baboons in Kenya

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**Background:** Diverse strains of simian immunodeficiency virus (SIV) infect over 40 species of African nonhuman primates (NHP) and continuously pose potential threat of transmission to humans. However, strain diversity amongst common free-ranging *Chlorocebus aethiops* (African green monkey-AGMs) and *Papio anubis* (Olive baboon) in Kenya remains unclear. For the first time, we investigated epidemiology and diversity of SIV in AGMs and Baboon from major Kenyan urban centres.

**Methods & Materials:** A total of 126 AGMs and 65 olive baboons from Mombasa, Kisumu and Naivasha were sampled once in situ and released. Blood samples were spotted on whatman FTA cards for DNA/RNA extraction. Total DNA from dried blood on FTA (DB-FTA) was subjected to PCR followed by high resolution melting (HRM) analysis using consensus primers targeting a 650-bp fragment in partial pol gene and a 900-bp fragment of env gene encompassing hypervariable V3–V5 regions.

**Results:** PCR-HRM analysis illustrated amplification of SIV fragments giving an overall infection rate of 30.95% (39/126) in AGMs and 3.07% (2/65) in Olive baboons. Subsequent sequence identification confirmed SIV infection in AGM and for the first time in olive baboon. Phylogenetic analysis of pol and env genes revealed extensive genetic diversity among newly generated SIVagm sequences within groups sympatric NHPs and within a geographical location. Signatures of pervasive and episodic diversifying selection were also detected on the env gene indicating continuous SIV diversification.

**Conclusion:** This molecular evidence of SIVagm in olive baboons illustrates continuous simian-to-simian SIV transmission in the wild and can be linked to potential risks of transmission to humans through consumption of monkey bushmeat. In addition, this study shows that DB-FTA specimens and PCR-HRM analysis can be used as a cost-effective alternative sampling method for the surveillance and monitoring of SIV and other retrovirus of public health importance.
Functionality of CD8+ T-cells in subjects under cART: implications on cure strategies

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Background: Reaching HIV cure will largely depend on the capacity of HIV-specific memory CD8+ T-cells (CD8TC) to eliminate the viral reservoir. However, CD8TC response is limited in subjects on cART. Here, we aimed to investigate the phenotype and function of in vitro expanded CD8TCs in HIV+ subjects and the impact of ART initiation timing on these parameters.

Methods & Materials: PBMCs from 28 HIV+ subjects on cART for 1 year were obtained. Twelve initiated treatment during chronic infection (Delayed Treatment, DT) and 16 within four months post-infection (Early Treatment, ET). PBMCs were stimulated with peptides spanning Nef and Gag plus IL-2 during 14 days. ELISPOT (pre and post-expansion) and Flow Cytometry (post-expansion) were performed to assess expanded CD8TC function (CD107a/b, IFN-g, IL-2, MIP-1b and TNF-a) and phenotype (CD45RO, CCR7, CD95 and PD1). Data was analyzed using non-parametric statistics.

Results: Magnitude of ELISPOT responses increased after expansion by $10^3$ times ($p<0.002$), in both groups, being this effect more pronounced in CD8TCs, compared to CD4TCs ($p<0.0001$), as confirmed by FC. Cells showed higher avidity after stimulation (evidenced by greater spot sizes, $p<0.002$). DT subjects displayed a broader response to HIV than ET, after expansion. ET group had a significantly higher proportion of monofunctional degranulating CD8TCs (CD107a/b+), when challenged against Gag peptides ($p=0.037$) compared to DT. Contrary, DT group showed higher polyfunctionality ($p=0.009$). In both groups, CD4TC responses were of lesser magnitude compared to CD8TCs and predominantly monofunctional. Bulk and HIV-specific CD8TC phenotype varied significantly between groups: ET subjects showed a preservation of stem and central memory cells while DT showed a fully-differentiated profile ($p<0.005$). When analyzing memory distribution within PD1+CD8+ cells, terminal effector were the most frequent subpopulation in DT and effector memory cells in ET individuals; evidencing a differential cell exhaustion profile in both groups.

Conclusion: We demonstrated that HIV-specific CD8TCs could be selectively stimulated and expanded in subjects under ART. We also showed that ART initiation timing has an impact on phenotype and function of CD8TCs, reflecting consequences of longer antigen persistence on immune function. Overall, results presented in this work have important implications for the development of cure strategies aim at boosting CD8TC responses.
Abdominal Tuberculosis Analysis of 110 clinical cases

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**Background:** In Argentina, more than 10,000 new cases of tuberculosis are produced annually and the abdominal form is infrequent. **Objective:** 1.-Describe the clinical and surgical characteristics, 2.- Search if there are differences in their presentation between the feminine and masculine gender in 110 cases of abdominal tuberculosis (AT) in patients V.I.H. negative assisted in a specialized hospital.

**Methods & Materials: Material and methods:** A retrospective analysis of 110 consecutive cases attended between 1993 and 2017 with the diagnosis of AT was made.

**Results:** Fifty-two patients were women and 58 were men. The average age was 38.4 years (range 14-69). The most frequent symptoms described were: weight loss (95%), abdominal pain (85%), hyperthermia (85%), diarrhea (20%), ascites (62%), palpable abdominal mass (13%) and anemia (97%). The chest X-ray presented alterations (56%) as pleural effusion or scarring lesions compatible with tuberculous pulmonary infection. Surgical findings were: peritoneum compromise (56%), abdominal adenopathies greater than 1 cm. (37%), compromise of the colon (37%), the proximal bowel and the distal ileum were affected in 33 (30%) cases, and in some cases the commitment was simultaneous. Laparotomy and laparoscopy were the most used methods for diagnosis. The overall mortality was 4 cases (3.5%) and the associated diseases were liver cirrhosis (13%) and chronic alcoholism in 16 (15.5%) cases. Culture was positive in 39 (35.5%) of the cases. Analyzed the differences between men and women it was found that women mean age was 32 years versus 49 in men and abdominal pain and colon involvement with statistically significant values.

**Conclusion:** The AT is a chronic, disseminated and serious disease. It should be suspected in patients with chronic symptoms of abdominal pain, fever, weight loss and anemia. In women, it occurred at an earlier age and with greater frequency of colonic compromise.
Evaluation of direct nitrate reductase assay for drug susceptibility testing of tuberculosis in a tertiary care hospital of Eastern Nepal

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**Background:** Emergence of multidrug-resistant tuberculosis is considered a serious threat to global tuberculosis control. Molecular methods are developed but are expensive and impractical for routine use in the resource-limited settings. Rapid detection of drug-resistant tuberculosis by direct nitrate reductase assay (NRA) aids in early diagnosis, appropriate treatment and reduction in disease transmission, particularly in countries with high tuberculosis burden. The objective of this study was to evaluate the performance of direct NRA for detection of rifampicin and isoniazid resistance in tuberculosis.

**Methods & Materials:** This is a comparative cross-sectional study conducted in the Department of Microbiology, Dharan, Nepal. A total of 100 new smear-positive sputum samples were processed as per the guidelines of revised national tuberculosis control programme, India. The performance of NRA was evaluated on Middlebrook 7H11 agar for detection of rifampicin and isoniazid resistance directly on sputum specimens and the results were compared with conventional proportion method. Sensitivity and specificity of the test were compared with the gold standard proportion method and Mc Nemar chi square test was used to find out the significant difference between two methods.

**Results:** The sensitivity of direct NRA for detection of rifampicin resistance was 91% and specificity was 100%, whereas, sensitivity and specificity of isoniazid resistance were 92.3% and 100% respectively. Agreement between NRA and proportion method was 99 percent for both the drugs. The mean days of drug susceptibility testing results were 19 days for NRA and 72 days for conventional proportion method. Around 95% of the samples gave positive results within 21 days.

**Conclusion:** Direct NRA on Middlebrook 7H11 agar is highly sensitive, reliable and cost-effective method for early diagnosis of drug-resistant tuberculosis. It has the potential to be implemented for rapid detection of multidrug-resistant tuberculosis in laboratories with limited resources.
1-hydroxy-5, 7-dimethoxy-2 naphthalene-carboxaldehyde inhibitors as novel antimycobacterial agents targeting H-InMyoFib cells and targeting enzymes involved in fatty acid biosynthesis of bacilli. 

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**Background:** Gastrointestinal tuberculosis (Gastrointestinal TB) is a rapidly common infectious disease in low income countries due to poor life style that poses diagnostic challenge, as the broad spectrum features of the disease which may lead to diagnostic interruptions and complications. Early diagnosis and initiation of antituberculous therapy without drug-resistance is essential to prevent morbidity and mortality.

1-hydroxy-5, 7-dimethoxy-2 naphthalene-carboxaldehyde (HDNC) is a bioactive compound derived from *Aegle marmelos* (Rutaceae, 'Bael'). It is a naturally occurring flavonoid having anticancer and wound healing properties.

**Methods & Materials:** The present study demonstrated that HDNC had ant-mycobacterial effects on tubercle bacilli ATCC25618, multi-drug and extensively drug resistant clinical isolates with minimum inhibitory concentrations of 147 and 312 μM, respectively. Bacilli mainly affect the GIT, causing a strong local inflammatory response that is critical to the pathogenesis of tuberculosis.

**Results:** We investigated the effects of HDNC on interferon (IFN)-γ-stimulated human GIT fibroblast H-InMyoFib cells. HDNC suppressed the release of tumor necrosis factor (TNF)-α and interleukin (IL)-12. A nontoxic dose of HDNC reduced mRNA expression of TNF-α, IL-1β, IL-6, IL-12, and matrix metalloproteinase-1 in IFN-γ-stimulated cells. HDNC inhibited IFN-γ-mediated stimulation of extracellular signal regulated kinase and p38 mitogen-activated protein kinase and showed high affinity binding to these kinases (binding constants: 3.95 × 10⁴ M⁻¹ and 6.8 × 10³ M⁻¹, respectively). HDNC inhibit targeting enzymes involved in fatty acid biosynthesis, such as enoyl-ACP-reductase, b-ketoacyl-ACP reductase and b-hydroxyacyl-ACP dehydratase of bacilli. A mouse in vivo study of lipopolysaccharide-induced GIT inflammation revealed that a nontoxic dose of HDNC reduced the levels of IL-1β, IL-6, IL-12, and INF-γ in GIT tissue.

**Conclusion:** Gastrointestinal TB is generally managed with medical therapy with antituberculous drugs. These data provide the first evidence that HDNC could be developed as a potent antituberculosis drug and represents as a strong candidate for the b-hydroxyacyl-ACP dehydratase enzyme of Bacilli.
Burden of diabetes mellitus among tuberculosis patients in Asia-Pacific region: Evidence from meta-analysis using real-world data

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Background: Burden of tuberculosis (TB) and co-morbid diabetes mellitus (DM) now a major public health problem. Tuberculosis-Diabetes Mellitus (TB-DM) patients have a higher risk of TB progression, relapse, and death as compared to TB only. The rising prevalence of diabetic cases globally is an alarming threat for rising cases of TB. So, this meta-analysis is aimed to understand the exact prevalence of TB-DM comorbidities in the Asian country.

Methods & Materials: An extensive literature search was done by two independent reviewers from inception to September 2017 in Pubmed, Web of Science, Embase, and Google scholar using a combination of keywords related to “diabetes” and “tuberculosis”. Articles were selected for inclusion on the basis of title and abstract screening in the first pass and full-text screening in the second pass. A Modified version of Newcastle-Ottawa Scale was used to judge the quality of the included study. The primary outcome was to estimate the pooled prevalence of DM among TB patients. Subgroup analysis was done by the stratification of the country. Cochrane Q statistics, p-value <0.10 and I² value >50% was considered statistically significant for heterogeneity. All the analysis was performed using comprehensive meta-analysis software v3.

Results: A total of 54 articles incorporating 57,771 TB patients were qualified for inclusion in this meta-analysis. Majority of the studies were of high quality. We found significant heterogeneity across the studies ($I^2 = 98.60\%$) so, random effect model was applied over fixed effect model. The pooled prevalence of DM among tuberculosis patients was found to be 18.4% (95% CI: 15.6% – 21.6%, $p=0.000$). Subgroup analysis revealed that pooled prevalence of TB-DM across Asia ranging from 8.9% (95% CI: 4.9% - 15.8%) in Srilanka to 33% (95% CI: 25.5% - 41.6%) in Iran. Almost similar burden were reported from India 19.8% (95% CI: 14.3% - 26.7%) and Pakistan 20.5% (95% CI: 11.6% - 33.6%).

Conclusion: We found a high prevalence of DM among tuberculosis patients in the Asian country. Tuberculosis management programme should consider early screening of DM among tuberculosis patients.
Post-natal cytokine levels of neonates of seropositive mothers and its implication in the vertical transmission of HIV and falciparum malaria

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Background: New trends in curtailing epidemiology of infectious agents include the immunological diagnosis. Studies have implicated increased plasma levels of TNF-α in clinical malaria and vertical transmission of HIV. Even though the intricate imbalances in cytokines levels threaten successful pregnancies especially among HIV and Malaria co-infected pregnant mother.

Methods & Materials: In the present study, pregnant women were polled-stratified for interview and subsequently enrolled in a longitudinal study for eighteen months in the endemic area of Saki. Blood samples were collected from mothers and epidemiological diagnosis of falciparum malaria was by microscopy while HIV was through serial protocol according to the standard algorithm. Spot Blood samples (2 mL) were collected for laboratory diagnosis of HIV and Malaria at delivery and post natal. The plasma concentration of cytokines: TNF-α, IL-2, IL-10 and IFN-γ was determined by cytokine ELISA techniques. Only IL-10 of the cytokines was pro-inflammatory while others were of anti-inflammatory.

Results: Forty-five (30.2%) of pregnant women were sero-positive with 63.3% seropositivity in their babies. The co-infection of HIV and Malaria rate was 22.8 % in pregnant women while 26.3% of their babies were co-infected. The levels of TNF-α was high (30.0´ 10^3 pg/µL) in non-infected babies at delivery whereas IL-2, IL-10 and IFN-γ peaked at (70´ 10^3 pg/µL, 40´ 10^3 pg/µL) and 16.0´ 10^3 pg/µL respectively in uninfected babies. At delivery, the levels of TNF-α, IL-2, IL-10 and IFN-γ was 18.3´ 10^3 pg/µL, 69.8´ 10^3 pg/µL, 41.0´ 10^3 pg/µL and rise to 28.3´ 10^3 pg/µL in co-infected babies. The level of IL-10 was highest in co-infected babies at the second month post-delivery. Also, there was a progressive increase in the level of IFN-γ at the third month among the un-infected, co-infected and seropositive babies.

Conclusion: The parasite density in co-infected babies in the first three months and the plasma levels of IFN-γ and TNF-α could be an indication of vertical transmission of both HIV and P. falciparum.
Tuberculous Meningitis – retrospective observational cohort in a university hospital
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Background: Although tuberculous meningitis (TM) represents near 1% of the cases of tuberculosis disease, it is the most severe form of tuberculosis, with high mortality rate.

Purpose: Description of tuberculosis meningitis cases and evaluation of infection outcome.


Results: During that period, 21 patients had a diagnosis of tuberculous meningitis, 81% (n=17) were males and the mean age was 52.6 years-old (min 22; max 84). More prevalent risk factors identified were: chronic alcoholism (>60g/day) in 23.8% (n=5), drug use in 14.3% (n=3) and iatrogenic immunosuppression in 14.3%. HIV infection was present in 28.6% (n=6).

On hospital admission, 23.8% (n=5) patients had a stage III on BMRC score (British Medical Research Council). Regarding the cerebrospinal fluid (CSF), the mean protein level was 2.06g/L (min. 0.30; max 4.53) and mean glucose de 0.34 g/L (min. 0.06; max. 0.81), mean pleocitosis of 233 cels/uL (mín. 0; máx. 911) with predominance of mononuclear cells (mean 140/uL; min. 0; max. 594). Microbiological diagnosis was based in PCR-assay (47.4%, n=9), followed by culture (38.9%, n=7).

There was concomitant pulmonary tuberculosis in 19.0% (n=4) of patients and 19.0% with disseminated disease. Tuberculostatic drugs were started in 20 patients (one died early) and 89.5% of them with adjunctive corticosteroids. External ventricular drain was needed in 42.9% (n=9). Ischemic stroke (28.6%; n=6) was the most common complication.

Mortality rate at two-years was 47.6% (n=10), with 6 deaths during hospitalization, 5 of them TM-related. At discharge, 9 of surviving patients had neurological sequelae with loss of autonomy.

Conclusion: Even though it was a rare diagnosis in hospitalized patients, TM had a high mortality rate with significant loss of autonomy.
Outcomes of HIV-associated pneumocystis pneumonia at a South African referral hospital
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Background: Pneumocystis pneumonia (PCP) is an important cause of community-acquired pneumonia amongst HIV-infected adults in sub-Saharan Africa. The clinical phenotype and outcomes of PCP are not well characterised, and have not been described in those admitted to intensive care units (ICU) in this setting.

Methods & Materials: We performed a retrospective study to assess the outcomes of patients with HIV-associated PCP at a South African referral hospital. Potential cases were identified through an electronic search of diagnostic test requests for PCP. We included patients over the age of 18 years with confirmed (any positive laboratory test) or probable PCP (defined according to the WHO/CDC clinical case definition). Cox proportional hazard models were constructed to identify factors associated with mortality.

Results: We identified 1878 test requests between 1 May 2004 and 31 April 2015; 124 cases (68 confirmed and 56 probable) were included in the analysis. Mean age was 36 years (SD 9) and 72% were female. HIV infection was newly-diagnosed in 44%. Median CD4 cell count was 26 cells/mm³ (interquartile range (IQR) 12 – 70), 83% were antiretroviral-naive, and 22% were on cotrimoxazole prophylaxis. There were no differences in baseline characteristics between those admitted to ICU (n = 42) and the general ward (n = 82), besides the arterial to inspired oxygen ratio (PaO2/FiO2, mmHg), which was lower in ICU patients (169 versus 233, p < 0.001). Overall 90-day mortality was 38.2% (95% confidence interval (CI) 29.9 - 47.2), and was significantly higher in those admitted to ICU (61.9% (CI 47.2 - 76.6) versus 25.9% (CI 16.4 - 35.5)). On multivariate analysis, PaO2/FiO2 < 100 and concurrent antituberculosis treatment were independently associated with inpatient mortality (adjusted hazard ratio 2.8 (CI 1.1 - 7.1) and 2.3 (CI 1.0 - 4.9), respectively). Median length of ICU stay was 13 days (IQR 8 - 19).

Conclusion: ICU mortality was high, but similar to high-income settings. Severe lung injury at presentation and concomitant antituberculosis therapy were independent predictors of worse outcomes, and could be included in ICU admission criteria for PCP in resource-limited settings.
Outbreak Investigation of Shigellosis Diarrhoea in Baudh District of Odisha-India 2016

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Background: Shigellosis is endemic in developing countries, estimated to cause 80 million cases of bloody diarrhoea including 0.7 million deaths annually. Odisha has reported four shigellosis outbreaks in year 2014-2015. In May 2016, an outbreak of shigellosis diarrhoea was reported in Baudh district, Odisha. We investigated the outbreak to identify risk factors and recommend control measures.

Methods & Materials: We defined a case as diarrheal illness (> 3 loose stools per day) in a person in Baunsuni village from May 1 – 15, 2016. We conducted active surveillance through house to house survey and conducted a 1:2 unmatched case control study to assess risk factors. We defined a control as a person staying at least two houses from a case without diarrheal illness. Faecal swabs and water specimen were collected and processed for culture at Regional Medical and Research Centre laboratory, Bhubaneswar.

Results: We identified 70 cases (60% female; median age 30 years [range 8-75 years]) with an attack rate of 3%. Consumption of overnight stored water rice (OR = 15, 95% CI = 4.76 – 47.21), fish (OR = 3.07, 95% CI = 2.25-4.19) and green leafy vegetables (OR = 3.1, 95% CI = 2.25-4.19) were risk factors associated with shigellosis. Two of four faecal specimens showed Shigella flexneri growth. E.coli was isolated in all water specimens indicating fecal contamination. All specimens were negative for Salmonella and Vibrio species.

Conclusion: This outbreak could be associated with food borne transmission and water contamination. Personal hygiene, frequent handwashing and proper food handling practice should be stressed among household to reduce food borne transmission. Improved water storage with disinfection could reduce future potential outbreaks.
The role of regional surveillance networks in enhancing global outbreak reporting
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Background: The Program for Monitoring Emerging Diseases (ProMED) is a moderated electronic reporting system dedicated to the rapid, global dissemination of outbreak reports. Its moderators are globally diverse, carefully selected, highly trained specialists. To improve cross-border communication and rapidly identify regional health threats, ProMED created regional networks where locally-based moderators use their access to local and regional medical and public health networks and media sources to obtain information not readily available outside of their region. In this analysis, we assess the impact of the establishment of ProMED’s Middle East/North Africa (MENA) and South Asia (SoAs) regional networks in April 2014 on ProMED’s outbreak reports for these regions.

Methods & Materials: Outbreak reports in countries within the two regions were extracted from ProMED’s database, and included country, disease name, species type, spatial coordinates, and report issue date. Data analysis included visualizing spatial information, identifying unique reports, and reporting trends per country and region. Data processing and analysis were conducted using R 3.4.0 statistical software. Rates of outbreak events per total number of ProMED reports per year were calculated to adjust for temporal trends in the total number of reports posted on ProMED. Rate comparison used a two-sided t-test; P <0.05 was considered statistically significant.

Results: The mean monthly incidence of ProMED reports concerning outbreaks in the MENA region increased from 28 reports (May 2012 - April 2014) to 83 reports after the establishment of the networks (May 2014 - April 2016), and from 29 reports to 101 reports concerning outbreaks in the SoAs region over the same time period. The number of reports per total number of ProMED reports increased by 259% for MENA, and 289% for SoAs (P <0.01). MENA reports most often addressed MERS (32.3%), foot-and-mouth disease (7.0%), avian influenza (6.7%), and measles (3.8%); whereas SoAs most often addressed dengue (14.9%), anthrax (7.3%), Japanese encephalitis (7.0%), CCHF (4.9%), and rabies (4.8%).

Conclusion: The establishment of MENA and SoAs regional networks with locally-based, expert moderators resulted in a significant increase in ProMED’s outbreak reports from these regions and an increased flow of disease information across regional borders and to the global public health community.
Characterization of 65 Babesia cases in Southeastern Pennsylvania, USA, from 2008 to 2016 with dramatic rise in 2015
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Background: The parasite *Babesia microti* is transmitted by ticks and causes a febrile illness. For decades it has been spreading outward from the northeastern USA. However, only 80 cases were reported 2005-2013 in Pennsylvania (mid-east coast USA, population 12,800,000). We report 69 cases from four hospitals of our healthcare system 2008-2016 with a striking rise in 2015.

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*No data before 2011*

Methods & Materials: After Institutional Review Board approval, charts with positive *Babesia* blood smears were reviewed. Of 69 total records, one was not available and three were outpatients only.

Results: The 65 reviewed babesiosis patients averaged 10.7 symptomatic days, often with nondiagnostic outpatient evaluations, before hospitalization. All patients had fever but physical examination and WBC were usually unremarkable. Low platelets were common (90% < 150,000, 79% < 110,000, and 67% < 100,000) and 68% had elevated transaminases. but sometimes only minimally. Concurrent Lyme Disease was very common (54% of 61 pts tested) and four patients had elevated cytomegalovirus IgM levels. “Mild-moderately ill” patients (34) averaged 4.0 days in hospital after starting *Babesia* treatment versus “severely ill” (31) averaging 8.1 days on inpatient therapy often with complications (severe anemia, heart failure, altered mental status, symptomatic splenic infarcts). The latter group was older (average 69.9 vs. 65.1 years), with immunosuppression, splenectomy, and/or multiple medical problems. Degree of parasitemia, especially > 4%, correlated with worsened severity of illness.

Conclusion: Babesiosis has been increasing in southeastern Pennsylvania with a marked rise in 2015 reflecting ongoing geographic spread. Also, more rainfall the year before led to increased acorn production and more white-footed mice which host disease-transmitting ticks. Concurrent Lyme disease was very common in our patients. Time to diagnosis improved as more *Babesia* cases were encountered but recognition of the significance of very low platelets could be improved and concurrent illnesses (especially anaplasmosis) were not always excluded.
Atypical clinical presentations of Neisseria Meningitidis Serotype W outbreak in military training school in Uganda, 2016; high proportions of pneumonia and conjunctivitis


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Background: On 23 November 2016, a trainee at Kaweweta Military Training School died of a sudden acute febrile disease. Autopsy showed purulent meninges, lung consolidation, unilateral pleural effusion and gram-negative diplococci on a meningeal swab. At the time, multiple additional trainees presented with pneumonia, meningitis and conjunctivitis.

We report epidemiological findings of an atypical meningococcal disease outbreak among military trainees in Uganda.

Methods & Materials: Probable case of meningitis was defined as sudden onset of fever in patient at the school from 1 November onward with ≥2 of the following: severe headache, neck stiffness, acute chest pain, restlessness or altered mental state. We defined conjunctivitis as case-patients with unilateral or bilateral conjunctivitis in the same period with or without meningitis or pneumonia. We conducted descriptive epidemiology, environmental assessment, bacteria culture of conjunctival pus swabs and RT-PCR on cerebral spinal fluid (CSF).

Results: Training at the school started on 18 October 2016. Between 1 November 2016 and 5 January 2017, 186 cases (three deaths) occurred among 3,147 trainees (attack rate=5.9%, 186/3147; case-fatality rate=1.1%). Four out of seven CSF specimens tested Neisseria Meningitis serotype W (MenW) positive by RT-PCR at Pasteur Institut, Paris France. Of case-patients, 80% (148/186) presented with clinical lobar pneumonia (8 with radiological evidence; 1 at autopsy); 18% (34/186) presented with acute meningococcal meningitis; 2.2% (4/186) presented with both. All the five school regiments (average regiment size 600 trainees) were affected (attack rate: 3.4–7.7%). No administrators or instructors (n=890) were affected. Women had a higher attack rate (13%) than men (5.7%). 124 trainee s had acute purulent conjunctivitis, of whom 89% (16/18) conjunctivae pus swabs yielded MenW by culture at Uganda National Public Health Laboratories. No trainee s had received MenW-containing vaccination. On average, each trainee had 0.59m$^2$ of sitting space and 0.77m$^2$ of standing. Mixing of trainee s from different regiments occurred constantly. Blood culture was not performed.

Conclusion: Atypical clinical presentation of Neisseria Meningitidis Serotype W meningitis outbreak occurred with conjunctivitis and pneumonia in a military school in Uganda. The extent of MenW pulmonary and ocular manifestations had not been reported before in this setting. Overcrowding and trainee mixing might have facilitated the outbreak.
Street Vendor Food - Dosa as a risk factor for a Food borne outbreak within Srilankan Refugee Camp, Tiruchirappalli Corporation, Tamil Nadu-India, 2017

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Background: Food borne infection resulted in 585 million gastroenteritis cases in 2010 and many outbreaks were not investigated systematically. A government hospital in Thiruchirapalli, India reported 32 cases of gastroenteritis from a refugee camp on 11 Jan 2017. We investigated to determine the source of the outbreak and to propose recommendations.

Methods & Materials: We defined a case as occurrence of ≥3 loose stools and vomiting within 24 hours among residents of refugee camp during 5-11 Jan 2017. We did matched case control study (1:2 ratio) by matching age, gender and neighborhood. We used semi-structured questionnaire to collect data on food and water sources. We calculated matched odds ratio (MOR) and 95% confidence interval (95% CI). We did unconditional logistic regression analysis after breaking matched variables to adjust for other confounders. We calculated adjusted odds ratio (AOR) with 95% confidence interval (95% CI). We collected 5 stools samples and tested for Vibrio cholerae, salmonella and shigella by culture. We assessed environment and collected 8 water samples.

Definition of dosa: A South Indian pancake made from rice flour.

Results: We identified 74 cases. Attack rate was 5.3% (74/1392), highest among 21-30 years age group (18% (22/119)) and no deaths. Outbreak lasted between 11 and 14 January with peak on 11th. Eating food from a local eatery was a risk factor (MOR: 10.2, 95%CI=3.6-28.9), while eating food served at temple festival (MOR: 0.14, 95%CI=0.04-0.50), eating ice (MOR: 0.41, 95%CI=0.12-1.44) or vada(MOR: 0.14, 95%CI=0.04-0.50) sold at streets were not significant. Unconditional logistic regression results proved that among food from street vendor food, consumption of dosa was associated with gastroenteritis (AOR=3.6, 95% CI= 1.4 to 9.3). All five stools samples were negative for Vibrio cholera, Salmonella and Shigella. Water distribution system was intact and all water samples were potable.

Conclusion: This gastroenteritis outbreak was due to consumption of dosa from a street vendor food. We educated public to avoid eating dosa from street vendor food. We sensitized the cook in street food vendor to practice hygienic cooking and storage of food.
State’s Preparedness for Coordination of Lassa Fever Outbreak Containment in Nigeria - April 2017

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**Background:** Lassa fever (LF), an acute viral hemorrhagic fever is endemic in Nigeria with annual recurrent outbreaks in different States and varying levels of mortality and morbidity. In order to prevent such episodes with better preparation for early detection and rapid control of the disease, the Nigeria Center for Disease Control (NCDC) evaluated Nigerian States’ level of preparedness with a view to defining areas with high disease burden and risk of outbreak. The aim of the study is to assess the level of preparedness for co-ordination of LF outbreak response activities across the states for informed decision and effective LF outbreak response, planning and implementing of high impact interventions.

**Methods & Materials:** A self-administered LF preparedness questionnaire was filled by 37 State Epidemiologists including the Federal Capital Territory to assess national preparedness. Data was entered, cleaned and analyzed using Epi-Info 7.2. States were stratified into Very High Risk (VHR), High Risk (HR) and Low Risk (LR) based on having ≥10, 1-9 or zero confirmed cases respectively in 2016 and 2017. State-specific level of preparedness, based on a three-staged scoring system was categorized into: Inadequate, 0-49%; fairly adequate, 50-74%; and adequate ≥75% preparedness. Variables of interest were summarized in frequencies and proportions.

**Results:** Six (16.0%) states were classified as VHR, 18 (49.0%) were HR, while 13 (35.0%). Twenty-six states (70.3%) had an Emergency Operations Centre (EOC) while 24 (64.9%) can activate their EOCs within 48 hours. Thirty-two (86.5%) have Emergency Preparedness and Response (EPR) Committees. A maximum of 3 (50%) of VHR states had functional EOCs, ability to activate EOCs within 48 hours and EPR Committees, when compared with 13-15 HR and 9-12 LR states, respectively. On the state-specific level of preparedness for co-ordination, 16 states (43.2%) were inadequate, 9(24.4%) fairly inadequate, and 12(32.4%) adequate.

**Conclusion:** Preparedness for co-ordination of Lassa fever outbreak responses should be improved in all the states, especially the VHR and HR states, to reduce morbidity, mortality, economic cost and psychosocial effect associated with LF outbreaks in Nigeria.
Outbreak of Crimean Congo Hemorrhagic Fever in a butcher family at Havaillian Abbottabad Pakistan, September 2015

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Background: Congo-Crimean Hemorrhagic Fever is a fatal vector borne zoonotic disease. Since identification of first case in Pakistan in 1976, sporadic cases have continued to occur. Animal movements before Eid-ul-Adha increasing propagation of ticks & disease risk. Health Department reported a case on Sept-9, 2015 and investigation started on Sept-11, 2015 with the objectives to identify risk factors and control the outbreak and to prevent disease transmission during Eid-ul-Adha

Methods & Materials: Using descriptive study design, case definition used was “a person from Havaillian/hospital staff who remained in contact with confirmed case or livestock and febrile for 14 days or less with hemorrhagic manifestations”. Samples tested using RT-PCR. Patients record, health and livestock data reviewed, hospitals staff and relatives interviewed using pretested questionnaire.

Results: All identified four fatal cases; father and three sons, were butchers by profession, presented with common symptoms; fever, hemorrhagic manifestations and body aches. The unique presentation of all four cases was with lower limbs paralysis and altered consciousness which was not been noted before in CCHF cases. Evaluation of the timeline of events showed common source infection. All identified contacts, 18 family members and 19 hospital staff, remained asymptomatic except four who developed fever; however their samples turned negative. Previous data revealed that disease is endemic in the district and record of livestock departments confirmed the presence of ticks in animals.

Conclusion: Late presentation of all four cases in hemorrhagic phase, resulted in death. Animal handlers are at high risk of getting infected due to poor knowledge. Strengthening surveillance, awareness and sensitization of animal handlers & health staff is recommended. Sensitization of first line general practitioners and hospital doctors in endemic areas is needed to identify the suspected cases in time.

In response to investigation and recommendations, the health department along with livestock departments, took preventive measures to control the outbreak. Media campaign was started in the area and all the country for the awareness of public to be careful during upcoming Eid. Advisories issued to reduce the chances of transmission due to gross animal movements before "Eidul Azha".
Seed Grants to Early Career Investigators in Low- and Middle-income Countries to Build Research Capacity in the Field of Infectious Diseases – Evaluating Grant Uptake and Reach

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Background: Low- and middle-income countries disproportionately bear the burden of infectious diseases. An essential element for reducing morbidity and mortality associated with these diseases is the provision of training, educational and research support to scientists confronting challenges in the countries most affected. The International Society for Infectious Diseases’ (ISID) Research Grants Program, first established in 1995, provides seed grants to early career researchers from resource-limited countries with the aim of building research capacity. To inform future funding strategies and assess the uptake and reach of the program, a retrospective analysis of ISID’s grant program was performed.

Methods & Materials: Data on the number of applications received and number of approved grants per year was collected. Demographic and academic information of the awardees was extracted from their grant applications and transferred into an electronic database (FileMaker Pro 16). Awardee information included gender, age at the time of the award, career level, title, institution, year of the award, project title, study area, study type, and mentor information. Descriptive data analysis was performed using Microsoft Excel to summarize and visualize the collected data.

Results: From 1995 through 2017, the ISID Research Grants Program awarded 156 seed grants ranging from 5,000USD to 7,000USD and the average number of applications per year increased from 62 (2002-2005) to 122 (2014-2017). Awardees represented 46 countries across 5 regions with most awardees coming from the WHO Africa region 42.31% (66); Americas 29.49% (46); and South-East Asia 13.46% (21). Fifty-four percent (84) of grantees were male, 46% (71) were female, plus one group application. The majority (78%, 118) were aged 30-40 years at the award. Most frequent project topics were HIV&TB (22.4%, 35), virology (20.5%, 32), parasitology (20.5%, 32) and bacterial infections (16.7%, 26). Study types included basic (32%, 50) and clinical research (68%, 106).

Conclusion: The Research Grant program achieved its goal of supporting projects from early career investigators in under-resourced countries around the world. Project topics focused on infectious diseases relevant to these countries. To fully understand the long-term impact of the grant program on awardees’ careers, an impact assessment using quantitative and qualitative data collected from awardee surveys is under way.
Relative consumption of Carbapenems among medical wards at an academic medical center
VCU Health System, Richmond, USA

Background: Antimicrobial resistance is a global public health crisis. This is especially true for infections due to gram negative organisms (GNOs). Carbapenems are some of the broadest spectrum antibiotics available and are often used to treat infections due to multi-drug resistant GNOs. However, carbapenem use has led to the widespread emergence of carbapenem resistance. Our study describes relative carbapenem use across medical wards at a tertiary academic medical center in the United States via the novel Proportion of Carbapenem Consumption (PoCC) metric. The PoCC can be utilized by Antimicrobial Stewardship Programs (ASPs) to assess for potential carbapenem overuse. Our institution did not restrict Meropenem usage by ASP pre-authorization during the study period.

Methods & Materials: A performance metric to compare the relative use of Carbapenems to Cefepime and Piperchlorin/Tazobactam (PT) known as PoCC was created. We examined the PoCC for medical wards at VCU medical center from August 2012-June 2017. Statistical data were created using the linear regression function of Microsoft Excel’s statistical package.

Results: We saw a significant decrease in the PoCC for one acute care medical ward (N9) across the study period. We did not see any other significant increases or decreases for the other wards during the study period. We did note a relatively high PoCC score on one medical unit (CCH3).

<table>
<thead>
<tr>
<th>Ward</th>
<th>Mean PoCC*</th>
<th>Slope</th>
<th>p-value</th>
<th>Mean Meropenem use (DOT^/1000 PDs^^)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematology/Oncology</td>
<td>0.241391</td>
<td>0.00060</td>
<td>0.361</td>
<td>76.5625</td>
</tr>
<tr>
<td>General Medicine (CCH3)</td>
<td>0.4147215</td>
<td>0.00073</td>
<td>0.335</td>
<td>100.9372</td>
</tr>
<tr>
<td>General Medicine (N5)</td>
<td>0.2341087</td>
<td>-0.00057</td>
<td>0.422</td>
<td>39.6864</td>
</tr>
<tr>
<td>Acute Care/Step down Medicine (N9)</td>
<td>0.2838209</td>
<td>0.00169</td>
<td>0.005</td>
<td>74.2003</td>
</tr>
</tbody>
</table>

^DOT = Days of Therapy; ^^PDs = Patient Days; *PoCC = [(meropenem DOT/1000 PDs)/(meropenem DOT/1000 PDs + cefepime DOT/1000 PDs + PT DOT/1000 PDs)]

Conclusion: Our study revealed a significant decrease in the PoCC on one acute care medicine ward over the study period. Additionally, a ward with a relatively high PoCC was identified. We believe the PoCC metric can be useful to ASPs in identifying hospital wards with possible carbapenem overutilization. More research is needed to investigate ideal use of the PoCC metric by ASPs.
Risk factors for healthcare associated infections caused by Carbapenem-resistant Enterobacteriaceae

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**Background:** Enterobacteria producing carbapenemase carrying the blaKPC gene spread rapidly and end up associating with a high mortality rate. Early identification of risk factors for Healthcare associated Infections caused by the blaKPC gene are responsible for the control of dissemination in the hospital environment. It is known that patients hospitalized in the Intensive Care Unit and in the use of antibiotics are more likely to develop infections when compared to non-exposed patients, however, there is as yet no consensus on which risk factors are directly related to this infectious disease. This study aimed to evaluate the risk factors associated with healthcare associated infections caused by enterobacteria KPC

**Methods & Materials:** It was a case-control study that consisted of a sample of 82 patients and 164 controls, totaling 246 patients, using a ratio of two controls for each case (2:1). The data were collected through an active search in the Automated Hospital Infection Control System, validated since 1993 by infectologists and statisticians and the electronic patient record.

**Results:** The results showed that patients previously colonized by gram-negative microorganisms (OR: 10.7, 95% CI: 2-60, p = 0.007), those with cancer (OR: 20.8, 95% CI: 4-120, p <0.001), those who were using invasive device (OR: 30.5, 95% CI: 2-382, p = 0.008), those with pressure lesion (OR: 136.2, 95% CI: 11-1623, p <0.001) and hospitalized in the Intensive Care Unit (OR: 1.4, 95% CI: 1.2-1.6, p <0.001) had a higher chance of developing healthcare associated infections caused by blaKPC gene than control patients. The area under ROC curve showed good overall performance (0.99, 95% CI: 0.992-0.998) of the final logistic regression model.

**Conclusion:** It was concluded that previously colonized patients, those with cancer, those who were using invasive device, those with pressure injury, and those who were hospitalized in Intensive Care Unit had a greater chance of acquiring infections caused by enterobacteria KPC when compared to those not exposed. It is inferred that these multiple causal factors can be minimized when infection prevention and control programs are implemented in the hospital environment.
Using Ozires, a Humanoid Robot, to Continuing Education of Healthcare Workers: A Pilot Study

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Background: Unfortunately, despite all the effort made by the professionals in infection control, compliance with hand hygiene practices is still unacceptably low, usually less than 50%. In Brazil, this rate of adhesion is 27%, varying between 12% before contact with the patient and 45% after this contact. Failure on educational interventions can be due to many factors. In this context, novel education strategies, more interactive, as the use of robot to personalize health education, can improve hand washing adherence. The objective of our study is to answer two questions: a) How to adapt a robot as MeccaNoid G15KS to be an instrument of health training and continuous education of healthcare workers? b) What is the effectiveness of the use of a humanoid robot on the compliance with hand hygiene?

Methods & Materials: Until recently, advanced humanoid robots were found in limited numbers due to high prices. They had prices between tens of thousands of dollars until more than million dollars, as Asimo (Smashing Robotics, 2016). MeccaNoid G15KS, a humanoid robot 122 cm tall, it was released as a toy in the beginning of 2015 (www.meccano.com/meccanoid). Nowadays it can be purchased for less than US$ 200 (www.amazon.com). Ozires was adapted with a mini projector to show video lessons and a kind of spy camera, to record people reaction when watching him.

Results: We can observe that the rate was stable, between January and July, about 36%, but, just after the introduction of Ozires, the rate increased to 65%.

Conclusion: Innovation is difficult to define, but, for sure to use a robot to engage medical and nurses in shortterm courses is a technological innovations in teaching and learning in healthcare facilities.
A retrospective survey of bacteraemia and advocacy for routine Salmonella immunization in children with sickle cell disease in north central Nigeria

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Background: Infection is a major contributor to morbidity and mortality in sickle cell disease (SCD). Together with hygiene and antibiotics, vaccination led to the elimination of many childhood infectious diseases and contributed to the increase in disability-free life expectancy that in Western societies rose from 50 to 78-85 years. Though it has been shown that individuals with sickle cell disease (SCD) are more susceptible to Salmonella infection, Salmonella vaccine is not included in the routine vaccination schedule for children in Nigeria. The objective of this study therefore is to determine the prevalence of Salmonella infections in SCD children compared to non-SCD children in Abuja with the aim of advocating for the inclusion of Salmonella vaccine to the routine immunization schedule of Nigerian children, especially children with sickle cell disease

Methods & Materials: A retrospective study of children enrolled into the Community Acquired Bacteremia among Young Nigerian Children Research (CABSYNC) over a 6 year period was done to determine the Salmonella isolates implicated in bacteremia of sickle cell disease (SCD). Blood culture and sickle cell screening results of a total of 5435 children aged 5 years and below were analyzed.

Results: Of the 5435 children, a total number of 370 positive blood cultures were reported, giving a 6.7% prevalence rate of bacteraemia, while 253 cases were SCD, giving a SCD prevalence rate of 4.7%. Of the 370 positive blood cultures, the frequencies of isolates are Salmonella Typhi (121, 32.7%), Non-Typhoidal Salmonella (42, 11.4%), Staphylococcus aureus (31, 8.4%), Pseudomonas spp (24, 6.5%), Streptococcus pneumoniae (17, 4.6%) and Enterococcus faecalis (20, 5.4%). Out of the 253 SCD cases, 16(6.3%) had positive blood cultures, out of which 7(43.8%) were Salmonella Typhi, 5(31.3%) were Non-Typhoidal Salmonella, 2(12.5%) were Enterobacter spp, 1(6.3%) was Streptococcus pneumoniae and 1(6.3%) was non-haemolytic streptococcus. Chi-square test revealed a statistically significant higher proportion of Typhoidal Salmonella within the SCD group compared to the non-SCD group (OR 2.804, p = 0.0613).

Conclusion: The result of this study shows that Salmonella is an implicated organism in bacteraemia among children with SCD, hence the need to include Salmonella vaccine into the routine immunization schedule for Nigerian children
Utilization of Educational Resources, Gaps, and Needs in the Area of Infection Prevention and Control Globally

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Background: The Guide to Infection Control in the Hospital (Guide) is a publicly available resource produced by the International Society for Infectious Diseases (ISID) since 1998 to assist in the prevention of infectious diseases. To improve the Guide user experience and identify gaps within the infection control landscape, an online survey was distributed to current Guide users.

Methods & Materials: In January 2017, an electronic survey was distributed to 8,055 registered ISID members who downloaded the 5th edition PDF version of the Guide. The survey contained 48 questions in the following categories: Availability of specific infection prevention and control (IPC) resources; availability of training in IPC; access to technology at the workplace; usage of the Guide and other resources in clinical work; and users’ needs for the next edition. Dichotomous questions, Likert scale-type questions, and open-and closed-ended questions were used in the survey. Conditional branching was applied to select questions.

Results: Respondents (n=1,121) from 194 countries representing all six WHO regions participated in the survey-Africa 16%(183); Eastern Mediterranean 9%(103); Europe 18%(206); Americas 29%(331); South-East Asia 19%(218); Western Pacific 7%(80). The majority of survey respondents were physicians 43%(488) followed by researchers 29%(323), and public health professionals 23%(259). In general, resource availability and usage varied between regions. Access to isolation gowns differed between regions; 15% (156) of African and 46%(114) of Latin American respondents replied “always available,” compared to 78%(173) of North American and 62%(175) of European respondents. In Africa, 84%(183) of respondents noted the use of a smartphone or tablet at the workplace, compared to 90%(126) in Latin America and 72% in both North America (205) and Europe (206) respectively.

Conclusion: The results of this survey demonstrate a wide variety of IPC resource availability, particularly between high and low-resource settings. To facilitate the implementation of effective IPC measures, simplified, step-by-step approaches that can be better adapted to under-resourced settings are urgently needed and should be included in future editions of the Guide. Our results demonstrate a large percentage of respondents across all regions utilize mobile technology in the workplace, providing opportunities for rapid distribution of up-to-date IPC content with wide reach.
Novel nosocomial variants of norovirus in pediatric healthcare settings

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Background: Prevalence of nosocomial enteric infections of viral origin in the non-infection hospitals remains underestimated now. In Russia the proportion of viral diarrhea in children ranges from 24 to 78%.

Methods & Materials: With the help of synromial diagnostics of acute viral infections we revealed 178 children in the large pediatric hospital of Nizhniy Novgorod city, including 138 individuals contracted non-infectious diseases of different localization. 68% were admitted to the department of endocrinology. We performed 1850 tests using real-time PCR (array AmpliSense OKI screen-FL, Moscow, Russia) in order to identify DNA (RNA) of rotavirus group A, norovirus, astrovirus, enterovirus, as well as DNA of adenovirus group F. 132 samples positive for viral acute diarrheal infections underwent: G[P] typing, genotyping by means of sequence determination with the Beckman Coulter machine; phylogenetic analysis of nucleotide sequences.

Results: The genotype G4P[8] prevailed in sporadic morbidity, and its finding in the hospital showed an importation of the virus to the healthcare setting. The presence of rotavirus G1P[8] is likely to indicate a sustainable transmission of the pathogen in the large multi-modal hospital. We also identified norovirus genotypes GI.1, GI.4 and GI.3. The hospital-acquired transmission is supported by the same place and time period of norovirus GI.1 been isolated, and identity of the nucleotide sequences determined. The norovirus GI.4 genovariant Sydney_2012 can be classified as a product of the virus evolution due to nosocomial circulation. Astroviruses were referred to as genotypes 1 and 2 without epidemiologic linkages.

We identified several important sequencies of the vial genome. They were deposited in the international database GenBank: KP208780, KP208781 (astroviruses), KP208782-KP208785, KR020053 (noroviruses), KR020054 (rotaviruses).

Conclusion: Our findings justify an active circulation of the enteric viruses (43.8% out of 178 patients examined) in pediatric multi-modal hospital. Molecular and genetic methods significantly increases efficiency of epidemiologic surveillance for viral diarrheal diseases.
First outbreak of Ralstonia mannitolilytica bacteraemia in patients undergoing haemodialysis at a tertiary hospital in Pretoria, South Africa

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Background: Ralstonia species are environmental organisms prevalent in different types of water supplies, including hospital water. Ralstonia species may cause serious infections in the immune compromised host.

This study describes interventions employed during an outbreak of Ralstonia mannitolilytica bacteraemia among patients undergoing haemodialysis at Steve Biko Academic Hospital (Pretoria, South Africa) nephrology department between May 2016 and July 2016.

Methods & Materials: Sixteen patients with R. mannitolilytica bacteraemia undergoing haemodialysis were identified. It was reported that the reverse osmosis pump in the dialysis water supply system was leaking. This is the main purification point of dialysis water in the system. The water then passes through a UV light source through to the ward. Water was collected for testing at the following points in the dialysis water system: at the point of entry, after passing through the reverse osmosis pump before the UV lights and from the ward (after passing the UV light).

Water samples were inoculated for enrichment in blood culture bottles. Once positive, they were plated on to blood, chocolate and MacConkey agar and incubated aerobically for 48 hours. Colonies were identified using the Vitek 2 (bioMerieux, France) system.

Results: The following organisms were cultured:
• At the point of entry: Bacillus spp and Stenotrophomonas maltophilia
• After the reverse osmosis pump and before the UV light: Ralstonia picketii, Sphingomonas paucimobilis, Cupriavidus pauculus
• After UV: Sphingomonas paucimobilis

Conclusion: Numerous organisms were cultured after passing through the reverse osmosis pump, indicating its ineffectiveness. The UV lights at the end of the system did have some effects in clearing organisms before they pass through to the ward. Ralstonia spp were not detected in the ward and may have been in numbers lower than the detection limit of culture. It was recommended that the dialysis water supply system be overhauled. Due to financial constraints, the system was only sanitised by passing a sterilant through the system. The reverse osmosis pump was also repaired. Regular (3 monthly) testing of water in the system was advised. UV lights in the system must be maintained on a regular basis. No further infections were noted in patients undergoing haemodialysis for the next 2 months.

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**Background:** Malaria among under-fives (U5) remains a priority issue that calls for global public health attention. Although much have been achieved in the past decade, there is still need to continuously review and monitor progress. The aim of this study was to determine the socio-demographic factors associated with malaria parasitaemia in children less than 5 years in Nigeria.

**Methods & Materials:** A secondary data analysis of the Nigeria Malaria Indicator Survey, 2015 was carried out. Data were extracted for U5 children tested for parasitaemia using Microscopy and Rapid Diagnostic Tests (RDT). Parasitaemia status was main outcome. Independent variables considered include child’s age, gender, residence, region, household wealth index, household size, gender of household head and use of ITN night before the survey. Data was analysed using descriptive statistics, chi-square and binary logistic regression at p < 0.05.

**Results:** A total of 6,050 U5 children were tested for malaria. Their mean age was 32.9 ± 15.5 months. All had RDT results analysed, but microscopy data for 285 (4.7%) children were not available. Overall prevalence of parasitaemia using microscopy and RDT tests were 27.3% (95% CI; 24.6 -30.2) and 45.1% (95% CI: 41.7 – 48.5) respectively. There was a significant association between age and prevalence rate ($\chi^2 = 21.477$, p <0.001). For both tests, prevalence decreased with increasing household wealth index ($\chi^2=16.9$, p = 0.002). Children from South-East region had least prevalence (4.4% and 6%, Microscopy and RDT respectively) while highest prevalence (43.3% and 41.7% for microscopy and RDT) was from the North-West region. Higher household size (≥ 7 members) was also significantly associated with higher prevalence for microscopy ($\chi^2 = 12.04$, p < 0.001), as well as RDT results ($\chi^2 = 19.54$, p < 0.001). Children residing in the rural areas were about 1.65 time more likely to have parasitaemia compared to those from the urban areas (OR: 1.6; 95% CI: 1.17 – 2.33).

**Conclusion:** Child’s age, residence, region and household wealth index, are key factors influencing burden of malaria among under-fives in Nigeria. Continuous education of caregivers, as well as control strategies designed to equitably allocate resources to most vulnerable populations are advocated.
Estimating the burden of disease and the economic costs attributable to Malaria in the Coffee-Triangle region of Colombia, 2007-2013

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Background: Malaria is still globally the main vector-borne parasitic disease and a significant public health threat in tropical countries. In Latin America, Colombia is still endemic and caused by three different species (Plasmodium falciparum, P. vivax and P. malariae). In its regions, such as the Coffee-Triangle, a significant morbidity is still associated. This would lead to a considerable cause of disability and economic burden but not studied before. There is lack of studies assessing malaria costs and disability in Latin America.

Methods & Materials: We calculated incidence rates of malaria during 2007-2013 in the Coffee-Triangle region of Colombia (an area constituted by 53 municipalities in three departments), using epidemiological data provided by Ministry of Health (active/passive surveillance system, SIVIGILA), and demographic data from its National Administrative Department of Statistics (DANE). The burden of disease was estimated through Disability Adjusted Life Years (DALYs) lost (according 2004 WHO methodology) and the costs (direct and indirect) were estimated based on the national recommendations for malaria management.

Results: There were a total of 8,978 cases during the study period, with incidence rates ranging from 0 to 33,703.08 cases/100,000 population (33.7 cases/1,000 API) in different municipalities (80% focused in one department, Risaralda). A total DALYs of 0 to 546.87 years lost/100,000 population was estimated, reaching up to 880.97 DALYs/100,000 population (upper limit of 95%CI). The study period estimated costs that were at least of US$ 1.92 million (max. US$ 2.59 million, upper limit of 95%CI).

Conclusion: Malaria is a parasitic, infectious and preventable disease, that can be presented as uncomplicated, mixed and complicated malaria, with recently severe disease criteria revised, then causing a considerable burden and costs. The costs and DALYs fluctuate as the incidence does, it is observed that they vary without showing a trend to increase or decrease which could mean that the burden and cost would, at least, not significantly decrease; with this in mind it must be considered working on evidence-based prevention strategies in order to mitigate these costs and burden, in the setting of malaria elimination programs, that consider Colombia in the near future.
Prevalence Study of Visceral Leishmaniasis among Stray Dogs in Meshkin-Shahr Endemic District of Iran

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Background: Canine visceral leishmaniasis as an endemic zoonotic disease is fatal in humans and dogs. CVL diagnosis is an significant step of visceral leishmaniasis supervision and control program in Iran. The aim of this cross sectional study was to determine the status of CVL among stray dogs as principal reservoir hosts.

Methods & Materials: Blood samples were collected from 68 dogs from June to October 2016 in Meshkin-Shahr district located in Ardabil province. Sera were separated from all peripheral blood samples and stored at -20 ºC until tested by direct agglutination test (DAT) for detection of anti-Leishmania infantum antibodies. The suspected dogs were euthanized and smears were taken from the spleens. All prepared smears were fixed in methanol and stained by Gimsa. Smears observed under a light microscope with a magnification of 1000X for the presence of amastigotes. Moreover, tissue samples were taken aseptically, from the spleen of the captured and dissected dogs and these tiny portions of spleen were cultured in two L. infantum special culture media: N.N.N. and RPMI 1640. kDNA-PCR was performed on seropositive samples including mass cultivated cultures and splenic smears. A 146 bp fragment in Kinetoplast DNA was amplified by means of specific primers of the L. infantum species RV1 and RV2 then DNA sequencing was done.

Results: Out of 68 dogs, 17 cases (25%) were seropositive at titers ≥ 1: 320. The result of kDNA-PCR was positive for three mass cultivated cultures and fourteen splenic smears. In kDNA-PCR the fragment of 146 bp were detected in three mass cultivated cultures and 14 splenic smears. The sequenced kDNA-PCR products were found 99% homology to L. infantum.

Conclusion: The results showed that dogs have an significant role in the upkeep of L. infantum in the endemic areas of visceral leishmaniosis in Iran. The necessity of using of serological and molecular tests is recommended for disease control strategy.
Comparative genome-wide analysis, expression profiling and interaction networks of different Zn finger families in Plasmodium falciparum provide new insights
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**Background:** Zinc (Zn) finger proteins (ZnFPs) constitute one of the largest and most diverse superfamily involved in a wide variety of biological functions. Despite significant reduction in malaria incidences, *P. falciparum* still remains more intractable human malarial parasite responsible for 99% malaria related deaths. In the present study, we report comparative genomic analysis of different Zn finger families in *P. falciparum* emphasizing expression patterns, protein-protein interaction networks and parasite specific structural features.

**Methods & Materials:** Different Zn finger families across *Plasmodium* species were identified by text search and HMM search using HMMER3.0 program. Functional classification of PfZnFPs was done manually based on PlasmoDB annotation and assigned orthologs annotation at UniprotKB. Subcellular localization was performed using either experimental evidences for PfZnFPs (ApiLocv3) or their orthologs or various online servers. Protein-protein interaction (PPI) networks were built using Cytoscape.

Expression profiling was done using MeV software. Real time PCR was carried out for 22 different PfZnFPs.

**Results:** Our genome-wide identification has revealed 18 different classes of Zn finger proteins in *P. falciparum* with a total number of 135 putative Zn finger family members. Notably, the most abundant Zn finger family across *P. falciparum* is RING finger followed by CCCH, C2H2 and PHD finger whereas in *Homo sapiens* C2H2 is the most abundant Zn finger family. Further, we carried out comprehensive genomic analysis of only four *P. falciparum* Zn finger subfamilies (PfZnFs) - RING (37), CCCH (29), C2H2 (24) and PHD (10). These PfZnFs were classified into 12 different subclasses based on functions and found to be mainly involved in ubiquitination, RNA processing, DNA replication and repair, cell cycle regulation and chromatin remodeling. Comparative transcriptome analysis of PfZnFs with already available datasets and RT-PCR data of 22 selected PfZnFs revealed a co-ordination between different datasets except some differences. By homology modelling, 3D structures of 13 PfZnFPs were predicted highlighting *Plasmodium* specific structural features. PPI analysis suggested an extensive network of putative interacting partners (more than 1500 PPIs) involved in several biological processes.

**Conclusion:** The present study provides new insights into the Zn finger family of *P. falciparum*, while opening new perspectives for further targeted advances.
Malaria Outbreak in Buhigwe District, Kigoma-western Tanzania, March 2017

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Background: On 20th March 2017, The Tanzania Ministry of Health received a report of 115 school children in Munyika Primary School of Kajana village in Kigoma Region who were reported to present with fever, headache and abdominal. The cause of the illness was unknown. The investigation team was sent to the affected area to verify and have control of the outbreak.

Methods & Materials: Suspected cases were defined as pupils of Munyika primary school who had presented with headache, abdominal pain with/without fever from 6th February- 23rd March 2017. We conducted a 1:1 unmatched case control study using structured questionnaire. Blood and stool samples were collected and tested using TaqMan PCR assay for all possible bacteria, protozoa and viruses. Data were entered, cleaned and analyzed using Epi Info version 3.5.4

Results: A total of 209 participants (104 cases and 105 controls) were enrolled in the study. Among the 104 cases, 70 (67.3%) were females. The mean age of both cases and controls were 12.7 ±1.8 years. Those who aged between 11 to 14 years consisted 50% of all cases and 67.3% of cases had fever. Among 104 cases, 67.3% tested positive for Mrdt. Of the 69 blood samples which were analysed revealed the presence of Plasmodium spp, Dengue virus and Bartonella spp by 75.4%, 4.3%, and 1.5% respectively. Analysis of 52 stool samples revealed presence of Blastocytis hominis, Schistosoma masoni, Giardia lamblia by 96.6%, 77.9% and 57.6% respectively. Not using mosquito nets was significantly associated with becoming ill [aOR=2.9, CI 1.29-6.38, p=0.009] and having mosquito nets at home was protective [aOR=0.35, CI 0.16- 0.78, p=0.01].

Conclusion: The cause of the illness was mainly due to Plasmodium spp (Malaria) however owning and use of mosquito nets were factors which were significantly associated with the illness. However enteric infections and other infections including Dengue virus worsened the outbreak. Preventive measures, mass testing and chemotherapy for Malaria, other Protozoa and Schistosomiasis should be conducted at Kajana village. Moreover more robust studies and surveys should be conducted at the village.
Adherence to malaria prophylaxis in Brazilian travelers

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Background: Among the infectious diseases, malaria is the main infectious cause of death and is also a major cause of morbidity in the returning traveler. Prevention is mostly based on mosquito repellent, impregnated nets and chemoprophylaxis. However, adherence to those measures is not always adequate.

Methods & Materials: To assess the adherence to the measures proposed to prevent Malaria in the travelers attended to the travel medicine center from the Federal University of Rio de Janeiro (Centro de Informações em Saúde do Viajante - Cives) and to study the causes of non-compliance, travelers, consulted by one of the doctors from the center between April, 2014 and November, 2015, were invited to participate in the study. Those who accepted were contacted by phone between 28 and 90 days after return and interviewed with the use of a semi-structured questionnaire to evaluate the adherence to mosquito repellents and malaria chemoprophylaxis. Reasons for non-adherence and adverse events were also inquired.

Results: Of the 86 individuals successfully reached by phone, 57 were prescribed chemoprophylaxis and 66 mosquito repellents. Doxycycline (54%), Mefloquine (42%) and Atovaquone-proguanil (4%), were the most common drugs prescribed. The complete compliance with chemoprophylaxis (not missing any dose) was 61%. Complete adherence to Mefloquine (78%) was significantly higher than to Doxycycline (45%) (p 0.026). The main reason stated for non-adherence was fear of adverse events. 19% of the travelers reported adverse events: 25% of those using Mefloquine and 13% using Doxycycline (p 0.21). There was no correlation between adverse events occurrence and non-adherence. The complete adherence to mosquito repellents was observed in 62% of the travelers and the mostly stated reason for non-compliance was absence of mosquitos.

Conclusion: Compliance to mefloquine was significantly higher compared to doxycycline and may be related to the fact that sleep disturbance, vivid dreams and anxiety were less disturbing than gastric symptoms presented for those taking doxycycline. Although fear of adverse events was the most reported reason for non-adherence, there was no association between its occurrence and non-adherence. Therefore, non-compliance may be based on traveler’s pre-conceptions that must be approached during travel counseling, to further ensure one’s compliance to preventive measures.
A polymorphism in the haptoglobin, haptoglobin related protein locus is associated with risk of human sleeping sickness within Cameroonian populations

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Background: Human African Trypanosomiasis (HAT) is a neglected disease targeted for elimination as a public health problem by 2020. Elimination requires a better understanding of the epidemiology and clinical evolution of HAT. In addition to the classical clinical evolution of HAT, asymptomatic carriers and spontaneous cure have been reported in West Africa. A genetic component to human susceptibility to HAT has been suggested to explain these newly observed responses to infection. In order to test for genetic associations with infection response, genetic polymorphism in 17 genes were tested (APOL1, IL1B, IL4, IL4R, IL6, IL8, IL12B, IL12RB1, IL10, TNFA, INFγ, MIF, HLA-G, HLA-A, HP, HPR and CFH).

Methods & Materials: A case-control study was performed on 180 blood samples collected from 56 cases and 124 controls from Cameroon. DNA was extracted from blood samples. After quality control, 25 samples (24 controls and 1 case) were eliminated. The genotyping undertaken on 155 individuals including 55 cases and 100 controls were investigated at 96 loci (88 SNPs and 8 indels) located on 17 genes. Associations between these loci and HAT were estimated via a case-control association test.

Results: Analyses of 64 SNPs and 4 indels out of 96 identified in the selected genes reveal that the minor allele (T) of rs8062041 in haptoglobin (HP) appeared to be protective against HAT (p = 0.0002395, OR 0.359 (CI95 [0.204±0.6319])); indicating higher frequency in cases compared to controls. This minor allele with adjusted p value of 0.0163 is associated with a lower risk (protective effect) of developing sleeping sickness.

Conclusion: The haptoglobin related protein HPR and HP are tightly linked and both are duplicated in some people and may lead to higher activity. This increased production could be responsible of the protection associated with rs8062041 even though this SNP is within HP.
Macrophage ghost entrapped Amphotericin B: A novel 'Trojan-horse' delivery strategy towards experimental Visceral Leishmaniasis

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Background: *Leishmania donovani* being an intracellular parasite poses many challenges against attempted chemotherapy. After the resistance towards the first line of antileishmanial drug, Amphotericin B (AmB) has been the treatment of choice against visceral leishmaniasis, a fatal tropical disease. However, unfavorable toxicity profile, severe side effects, prolonged parenteral administration procedure limit the use of Amphotericin B. Lack of available specific delivery system also makes this drug unsafe for the prolonged use.

Methods & Materials: AmB, DMSO, Methanol, MTT solution, Geimsa stain, Trypan blue dye, M199, RPMI-1640 medium, SDS electrophoresis components, Real time and semi-quantitative PCR components. In this current study, a 'Trojan horse' strategy based on macrophage-membrane derived nanovesicle has been introduced for carrying AmB. Membrane proteins of macrophage ghost play the crucial role in specific targeting of the *leishmania* infected macrophage, taking the route of the communication between infected and non-infected macrophages which is very crucial for the dissemination infection in host.

Results: Macrophage based nano-ghost loaded with AmB was synthesized and characterized by scanning electron microscope, further drug entrapment and release assay was assessed; where 89% drug entrapped and drug release was found significantly increase with time in DMSO/Methanol solvent. Antileishmanial efficacy was found ~4-5 folds better as compared to alone AmB in both promastigotes as well as in amastigote model. Pro-inflammatory cytokines were profiled and found increased expression of IL-12 and IFN-γ. These are very important molecular effectors that lead to inflammatory responses to control the growth of intracellular *leishmania*.

Conclusion: This cheap and biocompatible delivery vehicle has significantly improved the toxicity profile and lowered LD50 value of the drug compared to traditional way of its direct administration. Specific drug delivery was confirmed by presence of proteins on the surface of macrophage nano-ghost.
Virulence Factor RNA Transcript Expression in Cultured Clinical Isolates of Leishmania Does Not Vary by Host Age
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**Background:** Virulence factors (VF) are endogenous molecules that often enhance the pathogenicity of an organism. The role of host age on the immunopathogenesis of leishmaniasis is poorly understood. Despite pediatric populations being frequent victims of leishmaniasis, few studies elucidate whether or not age-specific disease progression patterns exist, on a molecular level in the parasite, whereas clinical epidemiological studies have noted some differences in prognosis and presentation in limited cohorts. Our objective was to quantify known VF RNA transcript expression in clinical isolates, and compare this across age groups.

**Methods & Materials:** Total cellular RNA was extracted from cultured promastigotes of *Leishmania*, cDNA was reverse transcribed, and qPCR assays were performed to determine transcript expression for: zinc-metalloproteinase (*gp63*), cysteine proteinase B (*cpb*), mannose phosphate isomerase (*mpi*), and heat shock proteins 23, 70, 83, and 100 (*hsp23*, *hsp70*, *hsp83* and *hsp100*). Sub-categorical analysis was conducted on a per-gene and pooled basis, between two age groups: pediatric (<18 years), and adults (>19 years).

**Results:** Four species isolated from 8 patients with cutaneous leishmaniasis are represented in this study: *L. infantum* (n=1, 12.5%), *L. tropica* (n=2, 25%), *L. V. braziliensis* (n=1, 12.5%) and *L. V. panamensis* (n=4, 50%). We did not observe differences in VF RNA transcript expression between pediatric and adult populations for the following: pooled VF (p=0.68), *cpb* (p=0.78), *gp63* (p=0.45), *mpi* (p=1.00), *hsp23* (p=1.00), *hsp70* (p=0.57), *hsp83* (p=1.00), and *hsp100* (p=1.00). The same analyses were done for the four *L. V. panamensis* clinical isolates, with no differences in VF RNA transcript expression: pooled VF (p=0.67), *cpb* (p=1.00), *gp63* (p=1.00), *mpi* (p=0.67), *hsp23* (p=0.67), *hsp70* (p=0.67), *hsp83* (p=1.00), and *hsp100* (p=1.00).

**Conclusion:** Here we describe initial quantitative evidence that suggests host age may not be a substantial correlate of VF RNA transcript expression in clinical *Leishmania* isolates. We failed to elucidate VF RNA transcript expression as the biological underpinning of age-based phenotypic associations suggested by clinical and epidemiological studies. The potential existence of novel or more host-derived immunopathogenesis mechanisms, rather than parasite-specific VFs, may be influenced by age.
YghJ (SslE), a cell associated and secreted lipoprotein of neonatal septicemic E. coli induces TLR2 dependent macrophage activation and proinflammation through NFκB and MAP kinase signaling

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Background: YghJ (SslE), a cell surface associated and secreted lipoprotein was identified as a potential vaccine candidate for extraintestinal pathogenic E. coli. We showed YghJ from neonatal septicemic E. coli could trigger secretion of various proinflammatory cytokines in murine macrophages, the signaling pathway of which is still obscure.

Methods & Materials: Cell surface receptor and down-stream adaptors of YghJ in murine macrophages (RAW264.7 cells) were identified by western blot and immunoprecipitation. Involvement of NFκB and MAP kinase in YghJ mediated cytokine secretion was determined using specific inhibitor against each signaling cascade and subsequent ELISA, immunoblot and immunofluorescence. Overexpression of iNOS was detected by RT-PCR. Production of chemokines was detected by RT-PCR and ELISA. Production of nitric oxide (NO) and reactive oxygen species (ROS) were detected by Griess assay and DCFDA staining respectively. Engagement of TLR2 was established using TLR2 siRNA knocked down RAW264.7. Flow cytometry was performed to detect overexpression of MHC II and co-stimulatory molecules on macrophages.

Results: We found that YghJ specifically binds to TLR2/TLR1 heterodimer on RAW264.7 and follows MyD88 dependent pathway. Pretreatment of macrophages with specific inhibitors against each signal molecule showed the involvement of ERK1/2, JNK1/2 and NFκB in secretion of IL-1 (IL-1α and IL-1β) and involvement of p38 and ERK1/2 in secretion of TNF-α in a TLR2 dependent manner as confirmed by using TLR2 knocked down cells. Moreover, our study unveils that YghJ can stimulate TLR2 dependent production of NO and ROS, which contribute to the anti-infection immune response of the host. Furthermore, YghJ produced M1 proinflammatory chemokines such as RANTES, MIP-1α and MIP-1β and increased expression of MHC-II and other co-stimulatory molecules (CD80 and CD86) on macrophages.

Conclusion: YghJ induces proinflammatory cytokine secretion in RAW via canonical pathway of TLR2 through NFκB and MAP kinase. The production of M1 chemokines, ROS and NO reflects that YghJ promotes activation and M1 polarization of macrophages, crucial in framing host’s innate immune response to this protein. Furthermore, over-expression of MHC-II, CD80 and CD86 hints that YghJ may skew the innate response towards Type 1 adaptive response supporting previous observation that YghJ can be a potential vaccine candidate in neonatal sepsis.
Chemical conversion of electrolytically generated pure HOCl to HOBr: analytical characterization of the reaction product, and its efficacy against scrapie prions and resistant microbes

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**Background:** Recently, we reported that pure, stable, electrolytically-generated hypochlorous acid (HOCl) inactivates prion proteins from humans (Creutzfeldt-Jacob Disease) and animals (e.g., Scrapie, Chronic Wasting Disease). Hypobromous acid (HOBr) has been shown to exhibit higher antimicrobial potency than HOCl against certain resistant organisms, including poliovirus, and to display this potency over a wider range of pH and temperature. Therefore, we hypothesized that conversion of our pure HOCl solution to HOBr might result in solutions with comparable or even higher potency and utility against infectious prion proteins and other microbes.

**Methods & Materials:** HOBr was synthesized from pure HOCl (pH 4) and sodium bromide. The pH of the solution increased to 5.7 with an ORP value of 992 mV. Raman spectroscopy detected a single peak at 618 cm⁻¹ corresponding to HOBr. HOBr concentrations determined by UV-Visible spectrophotometry in samples exposed to 22°C and 52°C declined with half-life values of ~32 and ~11 days, respectively.

**Results:** Real-time quaking-induced conversion (RT-QuIC) assays were used to measure the effects of exposure to HOBr solutions on hamster scrapie prions after 5 minutes: seeding activity was reduced by ~10³. The antimicrobial activity of HOBr was tested against spores of *Bacillus subtilis* and *Aspergillus niger*, and vegetative forms of *Staphylococcus aureus*, *E.coli*, and compared with that of HOCl preparations at the same molar concentration. Solutions were tested in parallel in timed suspension protocol exposures at room temperature. HOBr solutions showed antimicrobial effects on all target microbes. HOBr efficacy was equivalent or superior to HOCl for vegetative bacteria, was inconsistently higher against *B.subtilis* spores, and was always lower against spore forms of *A. niger*.

**Conclusion:** The results provide further evidence of the susceptibility of prion proteins to hypohalous acid inactivation, and confirm the potency of HOBr against certain resistant organisms, although they do not reveal obvious advantages over HOCl; in some instances the data reveal potentially important differences (e.g., fungal spores). They also demonstrate that aqueous HOBr is considerably less stable than pure HOCl; however, the higher pKa (8.7) of HOBr may yet prove advantageous in circumstances where higher environmental pH conditions will undermine the potency of HOCl.
The efficacy and safety of recombinant thrombomodulin on severe urinary tract infection induced disseminated intravascular coagulation; a retrospective comparative study

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Background: Urinary tract infection (UTI) complicates disseminated intravascular coagulation (DIC) when the disease becomes severe; mortalities of DIC is reported to reach to 37% despite current therapy. Cross-talk between the coagulation system and inflammatory reactions during severe UTI causes organ damage followed by multiple organ dysfunction syndrome or even death. Therefore, anticoagulant therapies have been expected to be beneficial in the treatment of severe UTI. Recombinant thrombomodulin (rTM) binds to thrombin to inactivate coagulation, and the thrombin-rTM complex activates protein C to produce activated protein C. The purpose of this study was to examine the efficacy and safety of rTM for treating patients with severe UTI induced DIC.

Methods & Materials: This study comprised 40 patients with severe UTI-induced DIC. All patients fulfilled the International Society on Thrombosis and Haemostasis criteria for overt DIC. The initial 20 patients were treated without rTM (control group), and the following 20 consecutive patients were treated with rTM (0.06 mg/kg/day) for six days (rTM group). The primary outcome measure was 28-day mortality. Stepwise multivariate Cox regression analysis was used to assess which independent variables were associated with mortality. Comparisons of Sequential Organ Failure Assessment (SOFA) score on sequential days between the two groups were analyzed by repeated measures analysis of variance.

Results: Cox regression analysis showed 28-day mortality to be significantly lower in the rTM group than in the control group (adjusted hazard ratio, 0.297; 95% confidence interval, 0.102 to 0.823; P = 0.027). SOFA score in the rTM group decreased significantly in comparison with that in the control group (P = 0.028). In the post hoc test, SOFA score decreased rapidly in the rTM group compared with that in the control group on day 1 (P < 0.05).

Conclusion: We found that rTM administration may improve organ dysfunction in patients with severe UTI induced DIC. Further clinical investigations are necessary to evaluate the effect of rTM on the pathophysiology.
Estimating Emergency Department performance decline attributable to overcrowding caused by seasonal influenza

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Background: Emergency Department overcrowding can lead to poor patient outcomes and increased mortality. We aimed to quantify the impact of influenza on national emergency access targets (NEAT) and premature patient departure in New South Wales, Australia.

Methods & Materials: This was a retrospective observational study of 11 million presentations to 115 hospitals during 2010 through 2014, using routinely collected administrative records. A time series generalised additive regression model was used to assess the correlation between weekly influenza activity and the weekly proportion of patients discharged in >4 hours and the proportion that departed before commencing or completing treatment ('did not wait'), after controlling for background, winter and other holiday effects.

Results: During 2011 through 2014, peak annual circulating influenza was associated with the peak weekly proportion of presentations discharged in >4 hours. The peak annual absolute weekly change in that proportion ranged from 1.52 (95% confidence interval CI. 0.89 to 2.15) percentage points in 2011 to 3.88 (95% CI 3.02 to 4.74) percentage points in 2014. This represented a relative increase of up to 13.0% attributable to influenza. For presentations that did not wait, peak influenza circulation was associated with statistically significant increases in all years, ranging from 0.60 (95% CI 0.22 to 0.99) percentage points to 2.68 (95% CI 2.31 to 3.06) in 2012. The maximum relative change was 43.3% in 2012.

Conclusion: Circulating influenza was associated with sustained increases and peaks in access block and premature patient departures. Influenza surveillance information is needed to guide Emergency Department demand management.

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**Background:** P24 and p27 gene represses Hepatitis B enhancers (pIIE1 & pIIE2) by inhibiting replicative property of HBV, hence accounting for the low serum levels of HBV DNA in co-infected patients. P27 additionally represses interferon-α motioning by meddling with janus kinase, tyrosine kinase 2, signaling transducer and activator of interpretation STAT1 and STAT2, which causes HBV replication hindrance. P24 & p27 gene is arguably considered to be major gene that underpins the incidence of HDV mediated HCC.

**Methods & Materials:** 100 whole genome sequences of all known genotypes of HDV were extracted from the NCBI and UNIPROT databases and subjected to multiple sequence alignment. The phylogenetic tree was reconstructed using the maximum likelihood method, employing 1000 bootstrap replicates. P24 and p27 gene was used to learn the structural and functional polymorphism. The two genes were imperiled to post translational modification analysis using expasy. One representative sequence was taken from each genotype and subjected to develop the molecular model using iterative threading and homology modelling. The models were subjected to structural and thermodynamic refinements and used to develop the potential based on geometrical complementarity. However, this information could further be exploited for designing disruptor/small inhibitor. Additionally, all sequences were predicted for the post translational modifications by different kinases to implicate their molecular and biological functions.

**Results:** Structurally, most part of p24 and p27 gene was found as intrinsically disorder providing rationale for its promiscuity for partner proteins ensuing multiple biological roles including carcinoma. Molecular modelling of the models shows considerable structural variations among different genotypes implying varying role in the HDV associated hepatocellular carcinoma. This observation is further strengthen by variations in the post translational modification profile. Post translation modification analysis showed kinases involved in the cell cycle regulation, DNA methylation, Histone modification and apoptosis tends to modify most of the sequences of gene pointing towards their role in carcinoma.

**Conclusion:** The present study provides first composite picture of the structural and functional polymorphism of p24 & p27 genes and their potential role in Hepatocellular carcinoma. Augmented with the further studies the present investigation may elucidate the potential targets for therapeutic intervention.
Emergent viruses in America: The case of Oropouche virus

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**Background:** Since 2014 the American Continent has seen the emergence and epidemic spread of Chikungunya and Zika viruses in a wave of febrile illnesses with consequences that we are still elucidating. In this scenario, a lot of effort has been implemented to characterize, describe, and anticipate pathogens that could appear as new epidemic threats. Oropouche virus is one of these candidates. It belongs to the family Bunyaviridae, is a negative-sense three-partite RNA virus that was isolated for the first time in 1955 in Trinidad, and it is known for causing extensive outbreaks in multiple regions of Brazil, Panama, and Peru.

**Methods & Materials:** We performed a systematic search for all the available published literature of Oropouche virus research in PubMed, Web of Science, and Google Scholar until August 2017, and reviewed the information related with the knowledge gaps of Oropouche virus especially those associated with its natural reservoirs, and its past and present-day distribution considering human outbreaks or epizootic detections.

**Results:** From the 189 articles retrieved, we built an updated, fully reviewed, and georeferenced dataset accounting for all the registered human outbreaks of Oropouche virus (75 localities, 52 [69.3%] in Brazil, 14 [18.6%] in Peru, 3 [4%] in Ecuador and Panama respectively, and 1 [1.3%] in Argentina, Bolivia, and Trinidad respectively). Moreover, we recorded all natural reservoirs were Oropouche virus has been detected (e.g., mammals [Bradypus tridactylus or Alouatta caraya], and birds [Columbina talpacoti]). Reservoirs have been detected in Colombia and Venezuela, countries in which human case reports have been lacking until the development of this study.

**Conclusion:** Oropouche virus research has received more attention in 2017 than in the previous years since its first published description in 1961; however, research regarding their pathogenesis and natural history has remained poorly addressed. Areas were Oropouche virus has been confirmed but were human cases remained undetected should be considered for active epidemiological surveillance to anticipate and prevent outbreaks, conduct serological surveys, or to develop prospective analyses aiming to elucidate the ecological drivers of Oropouche virus emergence and likely spread.
Hepatitis Delta Virus (HDV) Prevalence and phylogeny: An emerging health security threat in Pakis
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**Background:** Hepatitis delta virus (HDV) is a sub satellite RNA virus. It requires surface antigen of Hepatitis B Virus (HBV) for its transmission and causes chronic viral hepatitis. Its co-infection leads to the more severe form of chronic liver ailments as compared to HBV mono-infection, such as cirrhosis, hepatocellular carcinoma and liver failure. Furthermore therapeutic response is also peculiar and less satisfactory in these patients. This study was conducted to assess the prevalence of active HDV super infection & its phylogeny in HBsAg positive patients in Pakistan.

**Methods & Materials:** A total of 190 HBsAg samples were collected from all four provinces of Pakistan. In these 190 samples, 113 samples were from males and 77 samples were from females. Total RNA was extracted from these samples and screened for presence of active HDV infection by real-time PCR. HDV genotyping was performed by using PCR-RFLP method. Partial HAg fragment from 24 HDV positive samples were amplified and sequenced for phylogenetic reconstruction along with other reference sequences from GenBank.

**Results:** The results demonstrate the overall prevalence of active HDV infection to be 24.7%. The highest incident rate for HDV were from the Sindh with the infection frequency of 35% followed by 24% from Punjab, 20% from Baluchistan as well as 13.3% from Khyber Pakhtunkhwa (KP) respectively. Male gender and age group 21 to 40 years was found to be more infected with HDV. All of the 47 HDV positive samples were found to be HDV-genotype I which was further confirmed by phylogenetic analysis which revealed that all the sequences from this study belongs to clade I including three sequences closely related to geographical distant isolates from Turkey and Italy.

**Conclusion:** This study reports the high prevalence of active HDV infection in HBsAg positive patients specially from the province of Sind. Phylogenetic analysis revealed that the current circulating HDV strains have high genetic diversity and multiple origin of spread. Therefore, government & other international authorities should focus on this emerging pathogen & should take immediate preventive measures to control the spread of infection.
Prediction Models Using Machine Learning for Monitoring Severe and Fatal Hospital Cases of Influenza-like Illness – Implications of Emerging Epidemics or Pandemics in Future Years

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**Background:** Respiratory infectious disease is a global burden, especially during influenza epidemics and pandemics. Current approaches are not easy to predict prognosis from initial symptoms of influenza-like illness (ILI). A trustable prognostic information is important for clinicians and patients to make the best clinical management, as well as public health prevention measures in responding to outbreaks of influenza.

**Methods & Materials:** Accordingly, we initiated this study aiming to develop a machine learning based accurate prognoses prediction model for ILI cases. The dataset used in this study includes 103,010 events of ILI associated hospital admissions from Jan 2005 to Dec 2012 in Taiwan and the outcomes of concern include fatality and critical conditions. In this study, we employed two machine learning algorithms: decision tree and random forest. Meanwhile, the risk factors taken into consideration include age, sex, and underlying comorbidities.

**Results:** The models identified elderly patients had higher risk for morbidity and fatality. Major comorbidities identified in pediatrics and young adult patients were neurological and heart diseases. Middle age patients with diabetes, cerebrovascular, heart diseases or solid cancer had elevated risk. Both Decision Tree and Random Forest models showed similar performances for internal cross-validation, and in external data prediction. However, Decision Tree provided a user-friendly flow chart that is easy for the first-line healthcare workers to understand. The AUC of ROC in Decision Tree were 77.2, 77.0% for training and validation before pandemic, and 74.0% for testing during the 2009 pandemic periods.

**Conclusion:** Our study demonstrated that machine learning provides reliable prediction model in risk differentiation that can not only support clinicians to make the best decisions but also offer public health professionals to take early interventions. The models could be applied for emergency physicians to allocate hospital admission, as well as pandemic preparedness for better resource management to prevent ILI-associated complications and fatalities.
Population-weighted global seasonality of influenza

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**Background:** Influenza is considered a seasonal disease. Several studies examined influenza seasonality globally but provided conflicting results, used subjective methods, and did not consider population size at risk. This study described global seasonality of influenza weighted by population size, and by influenza type.

**Methods & Materials:** The World Health Organization's FluNet global influenza virology surveillance database was used; selecting countries reporting results in 95% of weeks, 2011 to 2016. Hemisphere and tropical nations were classified using the latitude of the national capital.

For each country, seasonality was defined as the proportion of annual influenza detections occurring in each week of the year, averaged over the six years. Prior to calculating proportions and averaging, the time series of weekly detections were smoothed using a 13 week (1/4 year) moving average to even out small counts. Then weekly proportions were calculated within each year. This standardised each year's proportions and prevented unusually high or low influenza years from over or under-influencing, respectively, the seasonal pattern.

After averaging the proportions across years, countries were aggregated globally, by influenza type, hemisphere and by tropical region, with weights applied according to 2014 population size.

**Results:** There were 69 countries with 95% of weeks complete, representing 78% of the global population. When weighted by population, influenza activity peaked (3.4% of annual activity) globally in week 7 (early February), with type A peaking in week 5 and type B in week 9. Minimum activity overall (1.1%) was in week 42 (mid-October). Temperate northern countries overwhelmed the global seasonal pattern. Temperate southern nations experienced peak activity in mid-July. Tropical northern countries had little seasonal pattern. Type B seasonality was markedly displaced from type A. India, Sri Lanka, Thailand, Bhutan, Philippines, Singapore, Ghana and Nigeria showed 2 distinct seasonal peaks. Tropical southern populations experienced influenza most during January to June. Results are shown in an animated world map.

**Conclusion:** This elegant analysis is more refined than previous influenza season studies and demonstrates the greatest population influenza risk by time of year. The greatest global population benefit may be achieved by vaccinating against influenza in September.
Respiratory infections by human Rhinoviruses in oncohematological and stem cell transplant patients: do they have the same clinical impact as other respiratory viruses?

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**Background:** Influenza A and B (Flu A/B), parainfluenza (PIV) and respiratory syncytial virus (RSV) cause lower and upper respiratory tract disease (LRD-URD) with significant clinical impact on patients with hematological malignancies (HM) or hematopoietic stem cell transplantation (HSCT). Rhinoviruses (HRV) are being increasingly detected in these infections, although their clinical impact remains a matter of debate. Our objective was to describe and compare clinical characteristics and outcomes of patients with HM and HSCT with LRD-URD caused by HRV versus non-HRV: Flu A/B, PIV and RSV.

**Methods & Materials:** Prospective observational study. We compared HRV (G1) vs. Flu A/B, PIV and RSV (G2) respiratory infections in patients with HM and HSCT between January 2013 and September 2017. Chi-square analysis and Kruskal-Wallis test were used for categorical and continuous variables, respectively.

**Results:** We enrolled 114 episodes: 45 in G1, 69 in G2. Both groups had patients with similar hematological diseases and stages, being lymphoma and acute leukemia the most frequent. Steroid therapy (20% vs 50.7%, \( p=0.001 \)) was significantly higher in G2, while use of biologic agents (40% vs 17.4%, \( p=0.007 \)), lymphopenia (33% vs 16.2% \( p=0.034 \)) and clinical presentation during preengraftment (20% vs 5.8%, \( p=0.032 \)) was higher in G1. Rhinorrhea was the most common symptom in G1 (71.1% vs 46.4%, \( p=0.009 \)). Other symptoms had similar frequencies in both groups. Over 50% of all infections presented as LRD (52% vs 50.7%, \( p=0.968 \)). Hypoxemia presented in similar rates (28.9% vs 27.5%, \( p=0.875 \)). The most common tomographic infiltrates were alveolar pattern and bilateral extension. In G1, co-pathogens in respiratory specimens were isolated in three patients (6.7% vs 0% \( p=0.053 \)) and other three had detectable plasma CMV viral load (6.7% vs 0% \( p=0.012 \)). Hospitalization was required in 58.8% of cases, with no significant difference between both groups. The 30-day overall mortality rate due to G1 and G2 infections were 6.7% and 7.2%, respectively (\( p=1 \)).

**Conclusion:** Patients with HM or HSCT and HRV infections had similar clinical picture and outcome to common respiratory viruses, with significant morbidity. Therefore, active diagnostic approaches are required, especially in patients with lymphopenia or use of biologic agents.
Immunodiagnosis of Echinococcus granulosus infections in humans of a Patagonian province, Argentina: comparison of two serological tests according to cyst location and genotype

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Background: The diagnosis of cystic echinococcosis (CE), a worldwide zoonosis, is based primarily on epidemiology, imaging and complemented by immunodiagnosis. Results of serology in human CE depend on factors such as location and genotype of Echinococcus granulosus cyst. Serology is no longer used in our province due to previous poor results. Location of human cysts may influence immune response, since antigenic stimulus may depend on organ implantation. Antigenic variability between genotypes of parasite could affect results of serological tests. E. granulosus is a species and genotypes complex and to date 8 genotype have been described. The aim was to compare sensitivity of two serological tests performed in CE patients, according to cyst’s location and genotype.

Methods & Materials: Patients with CE confirmed by surgery in a Patagonian province were evaluated between 2014-2017. Gender and age of patients, and cyst location were recorded. Serology was performed with two methods (ELISA and Rapid Immunochromatographic Test (RIT)). Cyst genotype was determined by amplification and partial sequencing of cox1 gene. Statistical analysis was performed with InfoStat.

Results: We evaluated 69 patients who harboured 104 cysts. Age ranged between 4 to 82 years. Location of cysts were: liver (33 patients), lung (24), bone (4), liver and peritoneum (4), kidney (2), retroperitoneum (1) and extrapleural (1). Cyst genotypes were: G1 (62.5%) and G6 (37.5%). Sensitivity of ELISA was 88.4% and 85.5% for RIT. Sensitivity of ELISA and RIT according to cyst location was: liver 90.9% and 78.8%; lung 87.5% and 91.7%; liver + peritoneum 75% and 100%; bones, extrapleural and retroperitoneum 100% and 100%; kidney 50% and 50%, respectively. Sensitivity of ELISA and RIT according to cyst genotype was: G1 cyst 88.6% and 91.4%; G6 cyst 95.2% and 85.7%, respectively.

Conclusion: Both method were adequate to detect anti E. granulosus antibodies in the studied patients with different locations and genotypes. However, RIT has an additional advantage since it is an easy, rapid and individual test. There were no significant differences in sensitivity between methods, which allows us to consider its application as a complement of hydatidosis diagnosis in our province.
Risk factors of Viridans Streptococci bloodstream infection in children with Acute leukemia: Case control study.

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**Background:** Viridans Streptococci (VS) bacteremia in patients with fever and leukemia has significantly increased over the last years. Risk factors described in this population include severe neutropenia, oral mucositis, administration of high-dose cytosine arabinoside, and antimicrobial prophylaxis with either trimethoprim-sulfamethoxazole or a fluoroquinolone. Literature on pediatric patients is scarce.

**Methods & Materials:** Case Control retrospective study. Patients with Acute Leukemia admitted between July 2016 and October 2017 in a high-complexity pediatric hospital were included. Patients with fever and VS bacteremia were defined as cases. Patients with fever were defined as controls. Two controls were included by each case. Predisposing factors, clinical and microbiological characteristics were compared. STATA 10 was used.

**Results:** n: 90 (30 cases and 60 controls). Fifty one (57%) were male. Mean age was 67 months (IQR 38-107). St mitis/oralis was the most frequent (27/30), followed by St. salivarius (2/30) and St. sanguinis (1/30). Out of 30 isolates of VS 10% exhibited penicillin resistance and 30 % intermediate penicillin resistance. Twenty percent of the strains were resistant to ceftriaxone. In bivariate analysis, AML (OR 6.8, 95% CI 2.5-18.2 p<0.001), severe neutropenia (OR 16.9, 95%CI 2.1-133.1, p 0.007), high doses cytosine arabinoside (OR 4.0 95% IC 1.6-10.4 p 0.004), oral mucositis (OR 2.9 95%IC 1.0-8.8 p 0.048) and intensive care unit requirements (OR 11.2 95%IC 2.2-57.2 p 0.005) were associated with VS bacteremia. No association with the use of central venous catheter, co-trimoxazole prophylaxis, previous antibiotics or viral coinfection was found. After adjustment by multivariate analysis, variables that remained associated with increased risk of VS bacteremia were AML (OR 6.8 95%IC 1.9-24.2 p 0.003), severe neutropenia (OR 10.1 95%IC 1.2-85.8 p 0.034) and oral mucositis (OR 7.3 95%IC 1.6-33.1 p 0.010)

**Conclusion:** The isolation of VS has become frequent in immunocompromised individuals. AML, severe neutropenia, and the presence of oropharyngeal mucositis were risk factors associated with VS in this study.
Mutational pathways of resistance to inhibitors of integrase (INIs) in patients treated with first generation INIs and their impact in Dolutegravir sensitivity.

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\textbf{Background:} First generation integrase inhibitors, Raltegravir (RAL) y Elvitegravir (EVG) have proven good efficacy and tolerability in HIV-1 patients. However, clinical studies showed that 60\% of highly experienced patients in virological failure develop mutations of resistance to INIs (MARS). The most frequently used INI in Argentina is RAL and it has three major mutational pathways: Y143CHR, Q148HKR and N155H. Both INIs have widely cross resistance, preventing their sequential use while the 2nd generation INI Dolutegravir (DTG), only has cross resistance in Q148HKR together with other secondary mutations. Patients under RAL/EVG accumulate secondary mutations and switch pathways. These events can reduce sensitivity to DTG and therefore, early detection of MARS is critical.

\textbf{Objectives:} Determine the prevalence and profile of resistance to INIs in experienced patients in virological failure to regimens including RAL or EVG. Establish the impact to DTG sensitivity for its sequential use.

\textbf{Methods & Materials:} We analyzed the genotypic profile of the integrase gene of HIV-1 in 67 highly experienced patients: 33 subtype B, 32 subtype BF and 2 subtype C. All patients were in virological failure to treatments including RAL (66) or EVG (1). RNA was extracted from plasma samples, amplified by RT-PCR of the entire gene (corresponding to 288 amino acids), sequenced and interpreted using the Stanford Database.

\textbf{Results:} 46 of the 67 patients showed primary mutations (69\%), together with secondary ones, except for 1 case. Six patients showed one or more secondary mutations: T66A (1), L74I (1), T97A (3), G163KR (4). The remaining 15 did not demonstrate MARS. The mutational pathways observed were N155H (24), Y143R (12), Q148HKR (9), E92Q (2). All secondary mutations observed were T66A, L74I, T97A, G118D, T121Y, A128T, E138AD, G140AS, V151I, S153F, E157Q, G163RK.

\textbf{Conclusion:} The high prevalence of resistance observed demonstrates that RAL has a low genetic barrier. The frequency of the pathways coincides with the literature and N155H is the most frequently selected. Since Q148H and Y143CR increase resistance and give replicative advantage, tend to replace N155H during treatment. Therefore, early detection is clinically relevant. Most of the patients (80\%) that failed to RAL/EVG remain sensitive to DTG.
Intestinal Carriage of Carbapenemase-Producing Organisms: Development of a sensitive and rapid molecular assay to detect \( \text{bla}_{\text{KPC}} \) and \( \text{bla}_{\text{OXA}} \) gene from fecal swabs

**Background:** Carbapenem-resistant microorganisms carrying carbapenemases are potentially a major global health problem. Intestinal carriage serves as a reservoir of carbapenemase-producing Enterobacteriaceae (CPE) and a source for cross-transmission in healthcare settings. Thus, infection control programs are essential tools to limit the spread of these pathogens. In this study, we developed a rapid and simple molecular method based on direct PCR from rectal swabs for detection of both \( \text{KPC} \) and \( \text{OXA} \) carbapenemases in hospitalized patients at our institution. Intended for being adopted by active surveillance systems, to limit the spread of antibiotic resistance and generate strategies for preventive management of intrahospital infections.

**Methods & Materials:** Touch Dawn Multiplex PCR (TD-PCR) was developed for detection of the \( \text{bla}_{\text{KPC}} \) and \( \text{bla}_{\text{OXA}} \) genes from rectal swabs. Two hundred fifty-two samples of rectal swabs were processed. Simultaneously, these swabs were cultured on Chromogenic medium KPC-CHROM agar and molecular detection of \( \text{bla}_{\text{KPC}} \) and \( \text{bla}_{\text{OXA}} \) genes for TD-PCR. The cultures were incubated 24-48 h at 35 °C, the colonies suspected of having resistance to carbapenems were confirmed by phenotypic and genotypic methods.

**Results:** We detected 31 positive (+) samples of total swabs (31/252) and 186 negative (-) samples by both methods. Additionally, twenty-five samples were positive by PCR and negative by culture. And 10/252 samples were culture positive and PCR negative, the presence of carbapenemases were not detected in seven of these samples (culture false positive). Usually reporting culture time was 48-72 hours, whereas for PCR time it was 4 hours.

**Conclusion:** The intestinal carriage screening for carbapenemase-producing organisms is an important tool in infection control programs. In conclusion, surveillance programs, using TD-PCR would increase sensitivity and decrease reporting times, contributing to control the risk of dissemination of the resistance mechanism and reducing the overall costs of isolation and hospitalization.
Impact of antimicrobial stewardship programs in public hospitals in Argentina.
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Background: Antimicrobial stewardship programs (ASP) are useful to fight antimicrobial resistance. We analyze the impact of ASP among public hospitals in Argentina.

Methods & Materials: Multicenter study with interrupted-time series design, comparing a pre- and post-intervention periods (PostIP) of 6 months each in 4 public hospitals with no ASP. The prevalence of selected resistant pathogens (SRP) causing nosocomial infections was determined: methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), extended spectrum ß-lactamase- (ESBL) and carbapenemase-producing enterobactariaceae (CPE), and multidrug-resistant Pseudomonas aeruginosa (MDRPA) and Acinetobacter baumannii (MDRAB). Antibiotic use (AU) was measured by defined daily dose (DDD) per 100 occupied bed-days (OBD) and reported in monthly median, in wards and intensive cares units (ICU). At month 7th, an ASP (post-prescription prospective audit modality) was started with restricted antimicrobials defined by each hospital.

Results: In the PostIP there was a non-significant decrease in the overall AU (-147 DDD/100 OBD; p=0.46), with a significant increase in general wards (+75; p=0.03) and a non-significant decrease in ICU (-171; p=0.4). Considering each antibiotic overall, the significant changes in AU were: increase of piperacillin/tazobactam (PTZ) (+53; p=0.01) and vancomycin (VAN) (+15; p=<0.001), and decrease of 3rd gen cephalosporins (3GC) (-31; p=0.02) and metronidazole (-11; p=<0.001). In wards, there was a significant increase in PTZ (+38;p=<0.001), VAN (+4;p=0.05), aminoglycosides (+9;p=0.01), and carbapenemes (+5;p=0.03), and significant decrease of 3GC (-14;p=0.02). In ICU, the differences were significant for VAN (+11;p=0.01) and metronidazol (-10;p=0.01). In one hospital the overall DDD/100 OBD reached statisticallly significant diminution (-49;p=0.05), in another there was a significant increase (+90;p=0.01), while the other 2 showed no significant difference (-254; p=0.17 and +21;p=0.19). We documented 1134 episodes of infections caused by SRP with no significant difference between the 2 periods. Overall, SRP in decreasing order of frequency were: ESBL, MRSA, MDRAB, MDRPA, CPE and VRE. MDRPA was the only with higher prevalence in the PostIP (p=0.013).

Conclusion: ASP in these hospitals did not significantly affect the AU nor the overall prevalence of SRP; however, partial positive results were obtained in some participating hospitals. Longer follow-up periods are required to better assess the potential benefits of an ASP.
Urine cultures: Inappropriate use. Economic impact in a public hospital. Retrospective study

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Background: Asymptomatic bacteriuria (BA) increases significantly in hospitalized patients, therefore the presence of bacteriuria is not an indication of urine culture (UC) request. The diagnosis of urinary infection (UI) associated with urinary catheter (UC) is the most frequent nosocomial infection.

Objectives: Define the conditions of the patients admitted to hospital to whom UC is released. Calculate the economic impact that implies the UC requested in an unnecessary way.

Methods & Materials: Quantitative, retrospective, descriptive and longitudinal study. Analysis of the UC archives in hospitalized patients from the period of January 1, 2016 to March 30, 2017 was carried out. The variables were: pathological background of relevance, presumptive diagnosis at the time of the request for UC, initial antimicrobial treatment directed at UI.

The data was processed through the INFOSTAT Software, with a descriptive statistic of frequency distribution.

Results: At the time of the UC 30% was requested with suspicion of UI by the attending physician; 4.7% were requested at the pre-surgical moment. The rest, (64.5%), was requested in the context of another diagnosis, the most frequent being the respiratory focus with 20%.

In 69% the treatment by the attending physician was not initially directed to UI due to suspicion of another infectious focus: UC was negative 65% and positive in 31%; whereas the economic cost is $ 500 with a positive result and $ 100 negative; we calculate the cost that implied: $ 79,500 for the negative and $ 32,900 for the positive, with a total: $ 112,400.

If we take into account that the final cost of the UC requested with criteria was $ 73,400, and the total cost of all was $ 176,800; it means that 58% of the total economic cost was for UC without clinical utility or diagnosis.

Conclusion: We consider it is important to optimizing these diagnostic methods will serve to reduce the financial expenses in health care.

It is also important to bear in mind that the positive data of the UC can lead to confusions by the attending physician when considering a BA as UI and thus to establish an inappropriate antimicrobial treatment.
Tuberculosis in patients with induced immunosuppression in an endemic country

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**Background:** The widespread use of immunosuppressive drugs has led to a growing population of patients with defects in the immune system, susceptible to opportunistic infections, such as tuberculosis (TB). The development of TB may be due to primary infection, reactivation or reinfection. Evaluation of previous TB and screening for latent TB could benefit these patients. The objectives of our study were to assess the history of TB in patients with induced immunosuppression, determine the prevalence of latent TB and describe the incidence of TB in the follow up.

**Methods & Materials:** Observational and prospective study (November 2015-October 2017). We included patients with immune-mediated inflammatory diseases before starting or with ongoing immunosuppressive therapy evaluated at the Infectious Diseases Unit of a public hospital of Buenos Aires City.

**Results:** We evaluated 266 patients, mean age 50 years (SD 14), female 79.7%. Underlying immunosuppressive drugs: methotrexate 41.7%, corticosteroids 19.2%, biological anti-TNF agents 13.5%, mycophenolate 9%, azathioprine 8.3%, cyclophosphamide 4.5%, tocilizumab 3.4%, rituximab 2%. Only 30.5% of patients were without immunosuppressive therapy at the first evaluation. The median of follow-up was 15.2 months (IQR 8-20).

In the initial evaluation, 17 patients (6.4%) referred a previous history of TB, all completed an appropriate treatment before being immunocompromised. The median of time of immunosuppressive therapy of these patients was 40 months (IQR 15.4-60). Neither of them developed TB during the immunosuppression. Latent TB was diagnosed in 16 patients (6.4%, 16/249), all were treated with isoniazid. None developed TB.

At the follow-up 4 cases of TB were diagnosed: 2 patients were in treatment with corticosteroids, 1 with adalimumab and 1 with methotrexate. Neither of them had evidence of latent TB at the baseline or previous history of TB. The incidence of TB was 1.5%.

**Conclusion:** In our study, the cases of TB occurred in the patients without previous history of TB or latent TB. Tuberculosis should be considered in all patients who will receive immunosuppressive drugs, especially in endemic countries, even in the absence of positive screening tests or prior history of this disease. Careful follow up should be warranted.
Assessment of Treatment of Carbapenem Resistant Enterobacteriaceae Expressing OXA-48 Carbapenemase
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**Background:** Gram-negative bacteria may cause complicated infections when resistant to antimicrobial agents, especially carbapenems. In the face of depleting treatment options, antimicrobial combination therapy has been utilized to manage such infections and to avoid the extensive use of toxic drugs such as colistin. However, the benefits of combination therapy over monotherapy have been controversial. As such, an alternative approach to treating carbapenem resistant infections is using β-lactam/β-lactamase inhibitor (BL/BLI) combinations. In this study, we assessed the efficacy of the novel carbapenemase inhibitor avibactam when combined with imipenem, meropenem, and ertapenem against several clinical Enterobacterial isolates that harbor the Class D carbapenemase OXA-48.

**Methods & Materials:** Five *Enterobacteriaceae* clinical isolates were screened for *bla*OXA-48. Minimal inhibitory concentrations (MICs) of carbapenems with corresponding β-lactamase inhibitors for each isolate were determined using broth antimicrobial microdilution testing. Efficacy of the most suitable *in vitro* treatment regimen of one of the isolates was tested on 30 BALB/c mice by infecting them with the isolate and treating them appropriately, then monitoring their survival for seven days. Reverse transcription real-time PCR analysis was performed to assess the molecular response of that isolate to the selected treatment regimen under both *in vitro* and *in vivo* conditions.

**Results:** The addition of avibactam to either meropenem or imipenem restored the susceptibility of the tested isolates to both antimicrobial agents. The addition of avibactam to ertapenem only restored susceptibility in one isolate, but managed to lower the MIC in the remaining isolates by an average of 67%. Survival studies in mice models revealed a marked increase in survival rates in those treated with meropenem in combination with avibactam, compared to those without the dual therapy. Meanwhile, RT-qPCR studies for both *in vitro* and *in vivo* settings respectively showed a significant increase in *bla*OXA-48 expression upon treating the bacterial isolate with meropenem alone or in combination with avibactam.

**Conclusion:** The use of β-lactams in combination with novel β-lactamase inhibitors is a viable alternative to antimicrobial combination therapy as it showed high efficacy *in vitro* and *in vivo*. β-lactam/β-lactamase inhibitor combinations used in this study should potentially being further assessed in clinical trials.
Residue and potential ecological risk of veterinary antibiotics in poultry manure in Bangladesh

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**Background:** The residue of Veterinary antibiotics (VAs) is becoming an obstinate health hazard and environmental problem in all over the world. However, residual levels of VAs, distribution pattern, usage are still obscure in developing domain like Bangladesh. This project systematically analyzed the usage pattern, occurrence, concentration and potential ecological risks of VAs residue in poultry manure in Bangladesh.

**Methods & Materials:** A questionnaire survey was conducted to understand farmer’s and prescriber’s perspective regarding VAs in poultry production and in manure. Both identification (by TLC) and quantification (by HPLC) methods were applied to screen four antibiotics namely ciprofloxacin (CIP), enrofloxacin (ENR), oxytetracycline (OTC) and doxycycline (DOX) in 120 poultry manure sample.

**Results:** All respondent farmers were multidrug users and only a quarter had residual knowledge (35.49%). However, most of them (86.08%) didn’t respect the withdrawal period. Sixteen different patterns of antibiotics of seven classes mostly (86.84%) critically important for human medicine were used. Poultry manure produced by these farms was used typically in agricultural field and fish pond (91.96%) and rest of 8.04% in biogas plant. Occurrence and concentration (mean±SD) of CIP, ENR, OTC and DOX are 40.83% and 28.81±20.85 mg/kg, 8.33% and 17.72±9.48 mg/kg, 23.33% and 16.50±11.48 mg/kg, 17.50% and 11.75±10.69 mg/kg respectively. The Hazard Quotient (HQ) value of OTC is 61.11, which resembles potential ecotoxic (since HQ>1 considered potential ecotoxic).

**Conclusion:** Overall, this work explores the perspective of VAs residue in farmers and prescribers and builds a foundation for potential adverse effect of VAs residue in antibiotics resistance phenomenon and in human food chain, and understanding ecological risk of VAs in Bangladesh.
In vitro antimycobacterial activity of 2-(((2-hydroxyphenyl)amino)methylene)-5,5-dimethylcyclohexane-1,3-dione: A new chemical entity against Mycobacterium tuberculosis

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Background: In our on-going efforts towards tuberculosis (TB) drug discovery programme, a high-throughput whole cell-based phenotypic screening of thousands of compounds against Mycobacterium tuberculosis H37Rv lead to the identification of a lead compound; 2-(((2-hydroxyphenyl)amino)methylene)-5,5-dimethylcyclohexane-1,3-dione (PAMCHD). In our earlier studies, it was observed that the test compound exhibited antimicrobial activity that was restricted to M. tuberculosis only. The test compound also proved to be non-toxic against a panel of human cell lines. Therefore, the present study was planned with an aim to further explore the antimycobacterial potential of the PAMCHD against M. tuberculosis H37Rv.

Methods & Materials: In this study, we determined the minimum inhibitory concentration (MIC) and Minimum bactericidal concentration (MBC) of the PAMCHD. Kill curve and drug interaction studies were performed. Effect of serum/protein binding on PAMCHD activity was explored. Further, post antibiotic effect (PAE), Mutation frequency (MF) and mutant prevention concentration (MPC) were studied.

Results: PAMCHD proved to be tuberculostatic (MIC, 2.5 µg/mL) as well as tuberculocidal (MBC, 5.0 µg/mL) agent. This compound was equipotent against drug resistant M. tuberculosis clinical isolates (MIC, 2.5-10µg/mL). The dynamics of M. tuberculosis killing revealed its time as well as concentration-dependent anti-TB activity with an Emax of 10.0 µg/mL (at this concentration M.tuberculosis culture were completely sterilized). PAMCHD acts synergistically and additively with key first line and second line ATDs respectively. PAE of PAMCHD’s was found to be 63.1 and 103.8 h at 4x and 8x MIC and that of INH (used as a control ATD) were 39.8 and 127.9 h respectively. MF for M. tuberculosis against PAMCHD was lower than that of INH at all the tested concentrations. The capacity of preventing emergence of resistant mutants of PAMCHD was found to be comparable to rifampin (RIF) as mutant MPC of both was observed to be 160µg/mL. MPC/MIC value of PAMCHD (i.e. 64) matched to the best-known value among ATDs (i.e. 68) exhibited by moxifloxacin reflecting its additional significant potential to prevent emergence of resistant mutants.

Conclusion: PAMCHD bears significant antituberculosis potential proven at various levels that warrant its further evaluation towards TB drug development.
Investigation of characteristics of residents in RCHEs associated with MRSA colonization after implementation of infection control training program


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Background: Residential care homes for the elderly (RCHEs) are considered potential reservoirs for transmission of Methicillin-resistant Staphylococcus aureus (MRSA). Infection control strategies have been introduced in RCHEs to curb the spread of MRSA. However, the effectiveness of these strategies in reducing MRSA is questionable. MRSA has remained prevalent in economically well-developed regions such as UK and the US despite the implementation of multiple intervention programs. We aim to investigate the characteristics of residents associated with MRSA colonization after implementation of common infection control strategies.

Methods & Materials: Residents from selected RCHEs in Kwai Tsing and Tsuen Wan district in New Territories West, Hong Kong were recruited from March 2011 to April 2012. They were interviewed about their health condition and nasal specimens for MRSA screening twice in the study period, with 2-13 months apart. Additional wound specimens were also collected if wounds were identified. Infection control intervention was represented by healthcare staff training and education in the study RCHEs between two screening tests. We defined subjects as being colonized with MRSA if either nasal or wound specimen was tested positive. A multivariable random-effect regression model on follow-up MRSA colonization status was applied.

Results: A total of 1832 residents from 32 RCHEs were recruited. The overall point prevalence of MRSA colonisation during the follow-up (after implementation of the training program) was 14.5%(265/1832). Upon adjusting for age, the model which best describes the association between follow-up MRSA colonization and health condition of residents includes the following characteristics: Low mobility indicated by Barthel Index 50 or below (adjusted OR=1.79;1.23,2.60), presence of skin conditions (adjusted OR=7.72;4.15,14.36), use of medical device (adjusted OR=2.25;1.55, 3.24) and presence of MRSA at baseline (OR=5.23;3.81,7.19).

Conclusion: We identified a strong association between health conditions of residents and MRSA colonization. MRSA colonization among residents with low mobility suggested that the service setting and environmental contamination may possibly be sources of MRSA transmission. Device care should be a crucial component in the strategic plan, as shown by the association of colonisation with the use of the medical device. Our findings highlighted the importance of the evaluation of intervention strategies for informing infection control policies.
Ertapenem as treatment for ESBL producing E coli prostatitis

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**Background:** Prostatitis presents one of the most common entities encountered in urologic practice. Treating ESBL producing enterobacteriaeecea urinary tract infections is a major problem especially in prostatitis because of the absence of active transporters for antibiotics and a relatively low prostate penetration of these drugs. Thus, therapeutic options are limited in infections with such resistant bacteria and require the use of carbapenems in the majority of the cases. Ertapenem is used in acute bacterial prostatitis yet not been approved by the FDA for this indication. The goal of this study is to compare the efficacy of ertapenem as to other antibiotics in the treatment of prostatitis with ESBL producing E. Coli.

**Methods & Materials:** It is a comparative retrospective study of the files of patients admitted in a tertiary care hospital between 1st July 2008 and 1st July 2014 treated for acute bacterial prostatitis caused by E. Coli producing ESBL with ertapenem and other antibiotics.

**Results:** The mean age of the 110 patients of this study was 69.58 years. Ertapenem was administered without previous efficient antibiotic treatment in 34 cases. 18.18% recurred in a period of three months. 85% of recurrences were caused by ESBL producing E.Coli (15.45%). 17% and 19% of patients treated with meropenem and imipenem respectively recurred in a 3 months period.

**Conclusion:** Ertapenem is as effective as other carbapenems in treatment of E.Coli producing ESBL and is not associated with a higher recurrence rate.
Resistance mutations and sequence types associated with extended spectrum beta lactamase, quinolone and aminoglycoside resistance in Enterobacteriaceae from South Africa. 

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**Background:** Antimicrobial resistance is now a global phenomenon requiring a coordinated international approach to amongst others, the surveillance of antimicrobial resistance. International data shows that there is significant co-resistance to extended spectrum beta-lactams, quinolones and aminoglycosides by *Enterobacteriaceae*. The presence of multiple drug resistance determinants has been shown to be transmitted horizontally by mobile genetic elements, where specific clones are identified. Sporadic reports from South Africa suggest global clones also circulate but the information is limited. The purpose of this study was to identify sequence types of important *Enterobacteriaceae* circulating in South Africa and the resistance genetic determinants carried by them.

**Methods & Materials:** This was a descriptive cross-sectional study of three hundred and eighty four consecutive, non-repetitive ESBL producing *Enterobacteriaceae* species collected from a referral laboratory. The phenotypic identification was confirmed by the MicroScan Walkaway automated instrument\textsuperscript{\textregistered}. Genetic determinants of antimicrobial resistance and sequence typing were elucidated by whole genome sequencing using the Ion Torrent platform. Assembled sequences were were annotated using the Resfinder search engine. Descriptive statistics using cross tabulations were used to analyse the data.

**Results:** The majority of ESBL, fluoroquinolone and aminoglycoside co-resistant isolates were *Klebsiella pneumoniae* species (57\%) followed by *Escherichia coli* (22\%). Other species identified were *Enterobacter cloacae*, *Citrobacter freundii*, *Proteus mirabilis*, *Morganella morganii* and *Serratia marcescens*. The beta-lactamase genes identified were *blaSHV*, *blaTEM*, *blaCTX-M*, *blaOXA*, *blaVEB*, *blaCMY*, *blaDHA*, *blaCMY* and *blaACT*. The *qnr*, *aac* and *oqx* quinolone resistance genes were also present. The aminoglycoside resistance genes identified were the *aac*, *aad* and *aph*. Trimethoprim-sulphamethoxazole and fosfomycin genes were also identified. The ST131 clone was the most common *Escherichia coli* sequence type identified although several other sequence types were identified in this species. In *Klebsiella pneumoniae*, there was no dominant sequence type. Sequence type ST152, ST1552 and ST234 were the most prevalent.

**Conclusion:** This study confirmed the global distribution of multiple-drug resistance in *Enterobacteriaceae*. Co-resistance with fosfomycin and trimethoprim-sulphamethoxazole was also detected, suggesting significant use in this country. The diversity in sequence types for both *Escherichia coli* but mainly *Klebsiella pneumoniae* was of concern suggesting circulation of possibly different mobile genetic elements. Identification of these mobile genetic elements is important.
Clonal dissemination of methicillin-resistant Staphylococcus aureus among hospital isolates and humans isolates and community's pets.

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**Background:** *Staphylococcus aureus* has become an important pathogen worldwide both in hospital and in the community. Its presence in the nasal cavities of healthy animals and humans facilitate its dissemination between healthcare and community settings. Methicillin-resistant *Staphylococcus aureus* (MRSA) have developed resistance to multiple antimicrobial agents complicating the clinical treatment of infections and have been increasingly reported among the general community in recent years. Thereby, molecular epidemiology studies are important and may help the elucidation of spread of Staphylococcus aureus. The aim of this study was to evaluate the clonal dissemination of *Staphylococcus aureus* strains among hospitalized patients (H-SA), community individuals (C-SA) and pets (Pet-SA).

**Methods & Materials:** A total of 170 *Staphylococcus aureus* isolates (112 H-SA; 31 C-SA and 27 Pet-SA) were typing by repetitive extragenic palindromic - polymerase chain reaction using RW3A primer (REP-PCR-RW3A). The cluster analysis was performed by using Bionumerics® software (version 6.5). Isolates showed belonging to the same cluster when the Dice correlation coefficient was ≥ 0.80.

**Results:** There were 61 distinct clusters among the 170 isolates. We highlighted six clusters that had both hospital and community isolates. Four clusters presented only methicillin-sensitive *S. aureus* (MSSA): a) three clusters with H-SA, C-SA and Pet-SA isolates and b) one cluster with C-SA and H-SA. In the other two clusters could be verified the spread of MRSA: a) one cluster with H-SA-MRSA and Pet-SA - MSSA isolates and b) one cluster with H-SA (MRSA), C-SA and Pet-SA (MRSA). Pet-SA MRSA presented the type II of genetic staphylococcal cassette chromosome mec (SCCmec type II) element, characteristic of hospital isolates.

**Conclusion:** The results showed a great clonal variability among *Staphylococcus aureus* isolates besides revealing the existence of clonal dissemination between animal and hospital isolates. The data demonstrated the versatility of this microorganism and warn of the fact that pets can be reservoirs of *Staphylococcus aureus* (including MRSA) facilitating its dissemination in the community.
Global risk mapping for major diseases transmitted by Aedes aegypti and Aedes albopictus
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Background: Aedes aegypti and Aedes albopictus are mosquitoes that can spread Zika, dengue fever, chikungunya and yellow fever; all diseases of major global public health importance. They also transmit important zoonotic viral diseases such as Rift Valley fever (RVF). These arthropod-borne viral diseases (arboviral diseases) have considerably widened their geographical range over the past five decades and are increasingly becoming a global concern.

Methods & Materials: This study extracts data from some of the largest contemporary databases relating to five arboviral diseases (Zika, dengue fever, chikungunya, yellow fever and RVF) and pairs these data with the known distribution of their vectors, Ae. aegypti and Ae. albopictus. The disease occurrence data for the selected diseases were compiled from literature dating as far back as 1952 to as recent as 2017. The resulting data sets were aggregated at country level, except in the case of the USA where state-level data were used. Spatial analysis was used to process the data and to develop risk maps.

Results: Out of the 250 countries/territories considered, 215 (86%) are potentially suitable for the survival and establishment of Ae. aegypti and/or Ae. albopictus. Ae. albopictus has suitability foci in 197 countries/territories while there are 188 that are suitable for Ae. aegypti. There is considerable variation in the suitability range among countries/territories, but many of the tropical regions of the world provide high suitability over extensive areas. Globally, 146 (58.4%) countries/territories reported at least one arboviral disease while 123 (49.2%) reported more than one of the above diseases. The overall numbers of countries/territories reporting autochthonous vector-borne occurrences of Zika, dengue, chikungunya, yellow fever and RVF, were 85, 111, 106, 43 and 39, respectively.

Conclusion: With 215 countries/territories potentially suitable for the most important arboviral diseases vectors and more than half of these reporting cases, arboviral diseases are indeed a global public health threat. The increasing proportion of reports that include multiple arboviral diseases highlight the expanding range of their common transmission vectors. The shared features of these arboviral diseases should motivate efforts to combine interventions against these diseases.
Perinatal Case Fatality Rate Related to Congenital Zika Syndrome in Brazil: a Cross-Sectional Study
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Background: Many studies have demonstrated a causal link between Zika virus (ZIKV) infection, microcephaly (MCP), and other congenital abnormalities (CA). This study aimed to determine perinatal case fatality rate in cases of Congenital Zika Syndrome (CZS) in the Rio Grande do Norte State (RN), a Brazilian Northeast State highly impacted by the Zika virus outbreak.

Methods & Materials: A cross-sectional study was conducted using data obtained through the State Health Department (SHD) for cases of MCP and CA in Rio Grande do Norte from April 2015 to February 5, 2016. Definition of perinatal period: commences at 22 completed weeks (154 days) of gestation and ends seven completed days after birth.

Results: During the study period, there were 486 cases of MCP and others CA notified in RN, of which 142 were confirmed and 108 remain under investigation. The remaining 236 cases have been ruled out by presenting normal examinations or due to presenting microcephaly by noninfectious causes. Of the total confirmed cases, 26.7% (38/142) died after birth or during pregnancy. 15.78% (06/38) of confirmed deaths had ZIKV infection during pregnancy and 2.63% (01/38) had a positive TORCH blood test. The six cases related to ZIKV were confirmed by RT–PCR and/or IgM/IgG antibodies against ZIKV. The remaining cases of deaths remain either under investigation or have been ruled out.

Conclusion: This study highlights a high rate of perinatal lethality (15.78%) in cases of CZS. Despite the growing number of CZS cases, the real incidence and prevalence might be higher due to the underreporting and lack of resources for confirmatory diagnostic tests (laboratory and imaging). Due to the high rate of lethality and the ongoing uncontrolled ZIKV outbreak, this study predicts an increase in the infant mortality rate in Brazil and highlights the need for developing public health programs to control the ZIKV outbreak. This study may be used to better describe the congenital Zika syndrome, its clinical outcomes and natural history.
Outbreak of Zika virus infection and the co-circulation of other arboviruses in State of Tocantins, Brazil.

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Background: Zika virus (ZIKV) is a re-emerging, mosquito-borne viral infection. Since 2015 the number of infected patients has increased significantly in South America. However, another arbovirus predominantly transmitted by Aedes aegypti mosquitoes can co-circulate in Brazil and cause similar clinical symptoms upon infection, complicating epidemiologic surveillance. In the first phase of the outbreak, patients with suspected Zika infection in Tocantins, during Jan 2015 – Ago 2016, we purpose this study to identify the epidemiologic and clinical characteristics of patients with ZIKV infections, and to make the differential diagnosis of Dengue virus (DENV), and Chikungunya virus (CHIKV).

Methods & Materials: In collaboration with the Tocantins Secretary of Health and the State's Central Laboratory of Public Health (LACEN-TO), we retrospectively analyzed 1338 serum sample results from patients that had illness symptoms compatible with Zika infection using Trioplex Real-time RT-PCR Assay. Data were analyzed using descriptive statistics extracted from clinical reports of the National System for Notifiable Diseases (SINAN) of Brazil provided by the Tocantins Health Department.

Results: Analyzed samples were from patients who were on average 31 years of age (range 0–100 years), 960 (72,4%) were female and 366 (27,6%) were male, all resided in Tocantins state. Diagnostic tests confirmed that 591 (44,2%) were positive for arbovirus. Of these 394 (29,4%) were positive for ZIKV RNA, 123 (9,2%) positive for DENV RNA and 74 (5,5%) positive for CHIKV RNA. Co-infection was also found between ZIKV/DENV (16 patients), ZIKV/CHIKV (10 patients) and CHIKV/DENV (2 patients). Clinical signs and symptoms were found for ZIKV in 331 (84%), for CHIKV in 36 (48,6%), and 58 (47,2%) for DENV.

Conclusion: In Brazil, Dengue outbreaks have been reported in practically all regions of the country since 1981. The recent emergence of both Chikungunya and Zika viruses has significantly expanded their distribution in Brazil. Our findings suggest that clinical and epidemiological criteria alone are not a good tool for ZIKV, CHIKV and DENV differentiation and reinforce the need for a better understanding of the co-circulation of these arboviruses and the possibility that individuals may become infected with more than one Aedes aegypti-borne virus at a time.
Discordant congenital Zika virus infection in dizygotic twins: a case report

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Background: Discordant clinical outcomes in congenital infectious disorders have been described, such as in Cytomegalovirus, toxoplasmosis and HIV infection, most of them in dizygotic twin pregnancies. In Brazil, since 2015, more than 2800 cases of congenital Zika infection (CZI) were confirmed. To date, three cases of discordant CZI infection in twins were reported, one case in monozygotic pregnancy and two cases in dizygotic twin pregnancies.

Methods & Materials: Here, we describe a case report with the clinical presentation of discordant twin siblings, one with microcephaly.

Results: Two boys, born in Salvador, Brazil, in June/2015, from a dizygotic twin pregnancy. The mother had rash and itchiness, in the seventh month of gestation. Through the obstetric ultrasonography, no abnormality was detected. The delivery occurred at a gestational age of 39 weeks, the first twin born with 2,240 g; APGAR 9/9 and the head circumference was 31 cm, with the diagnosis of microcephaly. Magnetic Resonance Imaging (MRI) was compatible with microcephaly, severe gliosis and ventriculomegaly. At 9 months, eye exam showed atrophy of the optic nerve bilateral. At one year and nine months of age, at the evaluation of the neurodevelopmental by Bayley III scale, cognitive, language and motor function were extremely low. This child had the diagnosis of Cerebral Palsy, by GMFCS V scale. Auditory evaluation by Brainstem Auditory Evoked Potential (BAEP) was normal at the age of two years. Anti-Zika IgG was positive. The second twin born weighing 2,685 g; the head circumference was 34 cm, APGAR 9/9. At one year and eight months, at the evaluation of the neurodevelopmental by Bayley III scale, cognitive and motor function were average and language function was high average. The MRI, eye exam, and BAEP were without abnormalities. Anti-Zika IgG was negative.

Conclusion: We described twins exposed to the Zika virus during pregnancy, but only one with neurological damage by CZI. Despite the advances in understanding the pathophysiology of CZI, little is known about the mechanisms enrolled in vertical transmission of the Zika virus. Possible factors, like fetus genetic factors, viral tropism, and the placenta barrier could explain this discordant presentation, but further studies are necessary to confirm.
Impaired quality of life after chikungunya virus infection: a 2-year follow-up study of its chronic inflammatory rheumatism in La Virginia, Risaralda, Colombia


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Background: Impact of post-chikungunya (CHIK) chronic inflammatory rheumatism (pCHIK-CIR) on Quality of Life (QoL) has been reported in some studies from La Reunion, France, India and Colombia. In this country our group published its consequence after 1-year of follow-up (Rheumatol Int. 2017).

Methods & Materials: In a cohort study among 62 cases serologically diagnosed in La Virginia, Risaralda, Colombia, followed-up by 2-years, demographic and clinical characteristics were collected at baseline. QoL status by 36-item short-form health survey (SF36) at 1-year and 2-years were assessed and compared. pCHIK-CIR cases were identified according to validated criteria (WHO/PAHO, 2015). Those with other arbovirosis during follow-up were excluded.

Results: Of the total CHIK-infected subjects in this cohort, 43 (69.4%) reported persistent rheumatological symptoms (pCHIK-CIR). All dimensions of SF36 as well as physical and mental component summaries were impaired in pCHIK-CIR+ compared to pCHIK-CIR- subjects. Differences in median scores between both groups, pCHIK-CIR- with 83.2% and pCHIK-CIR+ with 51.4%, were statistically significant (p<0.0001). In addition, in six dimensions, differences were also significant (p<0.05) (physical functioning [89.5%/62.1%], role physical [89.5%/39.0%], bodily pain [88.2%/44.4%], general health [77.7%/51.4%], vitality [79.5%/506%] and health transition [68.4%/40.7%]). When compared evolution from 1-year to 2-year, the more prominent reduction was found in health transition from 50.9% to 40.7%, as well bodily pain from 51.6% to 44.%. Global median scores reduced from 54.2% to 51.4%.

Conclusion: Despite possible cohort attrition bias, the comparability of pCHIK-CIR+- subjects allows the confirmation of a long-term impact of CHIK infection with less chance of returning to a previous health status. We observed sharp reductions in QoL not only during active pCHIK-CIR+ associated illness but also for several months and now more than 2 years after infection compared to healthy normal subjects that reached clinical recovery. This has implications for developing intervention programmes in countries with high risk of CHIK outbreaks but also to consider the long-term impact of CHIK infection in a significant proportion of infected patients, even more considering that in countries such as Colombia, after the 2014-2015 epidemics (with estimations of 3 million cases), transmission still occurs with >1,000 new cases in 2017.
Detection and molecular characterization of Chikungunya and Zika in a dengue endemic region of the Peruvian coast

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Background: Arboviral diseases have reemerged in the last years affecting primarily the coast of Peru. Piura is a region endemic for arboviruses where Dengue (DENV), Chikungunya (CHIKV) and Zika (ZIKV) have been previously reported. The aim was assess the presence of DENV, CHIKV, and ZIKV in serum samples of patients with acute febrile illness from Piura, Peru and describe associated clinical features.

Methods & Materials: A total of 496 serum samples from patients with acute febrile illness were collected from 18 primary care centers. All samples were analyzed via real-time RT-PCR to detect DENV, CHIKV, and ZIKV. In addition, positive samples for DENV were also processed for serotypes 1 to 4 classification via RT-PCR.

Results: DENV was the most common arbovirus detected in 170/496 (34.3%), followed by ZIKV in 39/496 (7.9%) and CHIKV in 23/496 (4.6%). Among the 170 samples positive for DENV, serotype 2 was the most predominant type present in 97/170 (57.1%) of samples, followed by the serotype 3 in 9/170 (5.3%). Headaches, muscle pain, and joint pain were the most common symptoms associated with fever in patients with DENV and ZIKV. No symptoms predominance was observed in patients with CHIKV.

Conclusion: DENV is considered the most predominant arbovirus in Peru and the number of cases have dramatically increased in the last 3 years. DENV-2 and DENV-3 are the most common serotypes circulating in Piura. In contrast to national surveillance reports, a higher prevalence of ZIKV and CHIKV have been observed in our population.
Potential impact of climate variability on the epidemiology of dengue at the Coffee-Triangle region of Colombia, 2007-2013
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**Background:** Despite emerging arboviral diseases, such as chikungunya and Zika, dengue continues to be the most important viral vector-borne disease in the world, particularly in Asia and Latin America, and is significantly affected by climate variability. The influence of climate in an endemic region of Colombia. The Coffee-Triangle region (constituted by 53 municipalities), from 2007 to 2013, was assessed.

**Methods & Materials:** Epidemiological surveillance data (weekly cases) were collected, and incidence rates were calculated. Poisson regression models were used to assess the influence of the macroclimatic variable ONI (Oscillation Niño Index) on the dengue incidence rate, adjusting by year and week. Monthly satellite images for total rainfall and surface temperature were obtained from the Tropical Rainfall Measuring Mission (1 month – TRMM) imagery database from NASA Earth Observations (NEO, NASA, USA) (http://neo.sci.gsfc.nasa.gov/) and were analyzed with Google Earth® software.

**Results:** Monthly variation of dengue rates in the region was: 0 to 684.90 cases/100,000 hab (Montenegro, Quindio, 2010). At nonlinear regressions, significant associations were found with ONI (p<0.0001), at municipalities of Quindio department: Calarcá (r²=0.7177), Armenia (r²=0.6287), La Tebaida (r²=0.6084), Montenegro (r²=0.4945) y Quimbaya (r²=0.4725); Caldas department: Chinchiná (r²=0.6834) and La Dorada (r²=0.6140); Risaralda: Pereira (r²=0.6245), Dosquebradas (r²=0.5678) and La Virginia (r²=0.5654). Risk climate GIS-based maps were developed.

**Conclusion:** El Niño significantly affected the incidence of dengue in the region. This association with climate change and variability should be considered in the elements influencing disease epidemiology. In addition, predictive models should be developed further with more available data from disease surveillance. This information should also be considered for studies relating to climate change and vector control. Finally the idea of these studies is to develop early warning systems, as has been proposed by the World Health Organization.
Modulating Immune Responses to Zika Virus Infection Through Dengue Virus Antibodies: An Epidemiological Analysis
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Background: Preexisting DENV antibodies may have a cross-reactivity against Zika Virus (ZIKV). A recent primate study suggested that prior DENV infection doesn’t adversely impact subsequent ZIKV disease and might be protective. This study evaluated the relation between the Dengue Fever (DF) outbreak in 2016 and the prevalence of ZIKV infection in Rio Grande do Norte (RN), a Brazilian northeast state endemic for arboviruses.

Methods & Materials: A cross-sectional analysis was conducted using data obtained through the RN Health Department from January 2015 to April 2017. We analyzed the epidemiological behavior of DF and ZIKV Infections in RN (last three summers).

Results: From January to March in 2015, 2016 and 2017 there were 6,902, 34,642 and 1,677 DF suspected cases, respectively. The number of confirmed DF cases in 2015, 2016 and 2017 were 523, 7,599 and 204, respectively. Regarding ZIKV infection, the number of suspected cases of between January to April during 2016 and 2017 were 3,486 and 86, respectively. The number of confirmed ZIKV infection in 2016 and 2017 were 97 and 0, respectively. Adding up the total cases of ZIKV infection which occurred during 2015 and 2016, we obtain a total of 14,584 (8,743 + 5,841). It represents less than 0.5% of the RN population.

Conclusion: This epidemiological evidence supports our hypothesis that the DF outbreak in 2016 has contributed to the decrease in the prevalence of ZIKV infection in 2017. It may be explained by preexisting DENV antibodies might partially neutralize ZIKV infection through serologic cross-reactivity. It supports the results found on the recent primate study. Our findings contradict the theory (based on in vitro experiments only) that previous immunity to DENV causes an enhancement of the immunological response in individuals exposed to ZIKV. Given the fact of the total suspected ZIKV cases in 2015 and 2016 represent less than 0.5% of the RN population, we cannot state that there are fewer Zika cases in 2017 because the population were previously immunized. These data are relevant from a public health standpoint given that regions which experienced ZIKV outbreak in Brazil are endemic for DF.
Towards a minimally invasive device for continuous monitoring of beta-lactam antibiotics

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Background: There is a need to develop novel mechanisms for monitoring and subsequently improving the precision of how we use antibiotics across care settings. We report the development of a microneedle array for the continuous monitoring of beta-lactam antibiotics.

Methods & Materials: A surface modified microneedle array was developed for monitoring beta-lactam antibiotic concentrations in human interstitial fluid (ISF). The sensor was fabricated by anodically electrodepositing iridium oxide (AEIROF) onto a platinum surface on the microneedle followed by fixation of beta-lactamase enzyme within a hydrogel. Calibration of the sensor was performed to penicillin-G in buffer solution (PBS) and artificial ISF. Further calibration was undertaken using amoxicillin, ceftriaxone, and amoxicillin-clavulinate. Open-circuit potentials were recorded and data analysed using the Hill equation and log(concentration [M]) plots. Sensor performance during continuous monitoring in human tissue was modelled by development of a physiologically inspired calibration rig mimicking antimicrobial perfusion through tissue. The test rig was used to determine the diffusion (D) and partition coefficients (K) of penicillin-G within the test rig set at an initial flow rate of 10 µLmin⁻¹.

Results: The microneedle sensor demonstrated high reproducibility between penicillin-G runs in PBS with mean Km (±1SD) = 4.4 ± 1.3 mM and mean slope function of log(concentration) plots 29 ± 1.80 mV/decade (r² = 0.933). Response was reproducible after 28 days storage at 4°C. In artificial ISF, the sensors response was Km (±1SD) = 7.7 ± 18.7 mM and a slope function of 34 ± 1.85 mv/decade (r²=0.995). Similar response was observed to amoxicillin. Ceftriaxone demonstrated a reduced but acceptable response. Addition of beta-lactamase inhibitor (clavulanic acid) inhibited response of the antimicrobial sensor to increasing concentrations of amoxicillin. Finally, the microneedle sensor was able to accurately respond to increasing and decreasing penicillin-G concentrations over a period of 2.5 hours on the test rig.

Conclusion: Our results suggest that microneedle array based beta-lactam sensing may be a future application of this AEIROF based enzymatic sensor facilitating advanced control of antimicrobial delivery. Further work is now underway to evaluate the performance of microneedle sensing in humans receiving beta-lactam antibiotics and develop closed-loop-control systems for optimisation of dosing.
FAST strategy - Find cases Actively by cough surveillance and rapid molecular sputum testing, Separate safely, and Treat effectively

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Background: Tuberculosis (TB) is believed to spread most efficiently in congregate settings such as hospitals, prisons and refugee camps mostly not from known TB patients on effective treatment, but from persons with unsuspected TB and this transmission is a driving force for global TB epidemic. FAST strategy- was developed within USAID TB Care II as an innovative approach to control this transmission.

Methods & Materials: Active cough surveillance at an entry point and immediate access to GeneXpert testing were key interventions of the FAST algorithm in Clinic’s in Georgia.

Results: Program was launched at the end of 2015 in two hospitals. 1565 unsuspected TB patients were tested with GeneXpert. Twelve percent (188 patients) of tested were confirmed with TB. Thirty five patients (2%) were found with Rifampicin Resistance. Each confirmed patient had on average three family members, who were also tested and 43 patients (7%) were TB positive. Mechanisms were established for reporting test results to National TB Program to ensure immediate initiation of effective treatment and awareness of family members for potential TB threat.

Conclusion: This experience showed that general hospitals and family members are at increased risk of TB transmission unless active TB case finding is in place targeted at patients with cough and chronic lung conditions. The FAST, as an effective strategy for preventing nosocomial transmission of TB, should be considered as a basic safety standard and incorporated into the national quality framework for all public and private hospitals through licensing or certification. Ministry of Health of Georgia is planning on placing GeneXpert diagnostic machines in all major hospitals in Country from 2018.
Polymorphisms of the IL-10 and IL-1β genes influence toxoplasmic retinochoroiditis, São Paulo, Brazil

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Background: Toxoplasma retinochoroiditis caused by the protozoan *Toxoplasma gondii* is the most common form of posterior uveitis with a prevalence of 27.0% of patients with ocular diseases in our outpatient clinic. The immune system, regulated by polymorphisms of the inflammatory cytokine gene, *IL-1β*, and the anti-inflammatory gene, *IL-10*, has been associated with clinical manifestations of ocular toxoplasmosis.

Methods & Materials: This study investigated the effect of the -511C/T polymorphism of the *IL-1β* gene and the -1082G/A polymorphism of *IL-10* gene in patients with toxoplasmic retinochoroiditis. Three hundred and twelve patients were analyzed - Group 1 (G1): 110 patients (54.5% male) with IgG+ for *T. gondii* and presumably with toxoplasmic retinochoroiditis; Group 2 (G2): 104 patients (48.0% male) with IgG+ for *T. gondii* but without toxoplasmic retinochoroiditis and a control group (G3): 108 patients (50.9% male) with IgG- for *T. gondii*. The gene polymorphisms were identified by PCR-RFLP.

Results: The mean ages of the subjects in G1, G2 and G3 were 42.7 (range: 21.4-72.7), 56.9 (range: 17.0-56.9) and 35.2 (range: 13.6-35.2) years, respectively. On identifying the -511C/T polymorphism of the *IL-1β* gene, the frequency of the TC genotype was higher in G1 compared to G3 (p = 0.05; OR = 1.95; 95% CI: 0.99-3.91) and the frequency of the CC genotype was lower in G1 compared to G2 (p = 0.02; OR = 0.30; 95% CI: 0.10-0.88). There was a higher frequency of the TT genotype in G3 compared to G1 (p = 0.01; OR = 0.38; 95% CI: 0.17-0.84). The comparison of the genotypes of the *IL-10* -1082G/A polymorphism G1 + G2 vs. G3 (p = 0.061; OR = 6.551; 95% CI: 0.774-55.413) indicated that the GG genotype is a risk factor for this infection; the G and A alleles do not influence infection or disease (p = 0.846; OR = 1.039; 95% CI: 0.710-1.521).

Conclusion: The -511C/T polymorphisms of the *IL-1β* gene and -1082G/A polymorphisms of the *IL-10* gene influence, respectively, the development and protection against toxoplasmic retinochoroiditis in the population studied.
A new rapid test device to improve the usability of current Dengue NS1 Ag STRIP for Dengue diagnosis

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Background: A new generation of test in cassette has been developed to improve the usability of the current Dengue NS1 Ag STRIP (Bio-Rad Laboratories, USA). It allows its storage at 2-30°C and an additional application in blood specimen. The aim of this study was to evaluate its analytical performances and robustness.

Methods & Materials: Performances, anticoagulant impact (EDTA, Heparin, Citrate) and robustness were assessed using serum/plasma or whole blood specimen from French blood donors and frozen documented sera for potential cross reacting diseases. Positive samples were prepared by spiking the specimen with recombinant NS1 protein of the 4 Dengue virus (DENV) serotypes expressed in human cells. Limit of detection (LOD) of the new Bio-Rad RDT Dengue NS1 Ag assay was compared to that of the current Dengue NS1 Ag STRIP and to SD Bioline NS1 rapid test. Robustness in “tropical” conditions of use was assessed using an oven (37°C and 85% hygrometry).

Results: Specificity of the RDT Dengue NS1 Ag assay using plasma (n=150), serum (n=69), venous (n=100) and finger stick (n=20) whole blood was 100% (95%CI: 98.9-100). No cross reactions were evidenced with Chikungunya (n=10), Yellow Fever (n=10), Zika (n=10), West Nile Virus (n=5), Malaria (n=10), HIV (n=11), HCV (n=10), HAMA (n=10), ANA (n=10) or RF (n=10) positive samples except for 1 RF sample also found positive with the Dengue NS1 Ag STRIP. LOD was in the same range as that of the current Dengue NS1 Ag STRIP assay in plasma and of SD assay in whole blood [5ng/mL-26ng/mL]. There was no significant difference between intensity of the test lines obtained in “tropical” versus normal laboratory conditions of migration and between the 3 tested anti-coagulants in whole blood specimen (Friedman test, n=10, p=0.16 and p=0.22, respectively).

Conclusion: This study shows that the performance of the new RDT Dengue NS1 Ag device for Dengue NS1 Ag detection should be as reliable as that of current Dengue NS1 Ag STRIP assay. The additional whole blood application, the cassette format and new storage conditions improve its usability. Clinical trials are in progress to complete these data.
The role of the gene CCR5 polymorphisms CCR5∆32 and CCR5 59029 in ocular toxoplasmosis.

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Background: C-C chemokine receptor type 5 (CCR5) is responsible for recruiting cells from immune systems to the inflammation areas. This study aimed to determine whether the CCR5∆32 and CCR5 59029 A/G polymorphisms are associated with the development of ocular toxoplasmosis in humans.

Methods & Materials: 480 patients recruited were separated into two groups: “with ocular toxoplasmosis” (G1: n = 160) or “without ocular toxoplasmosis” (G2: n = 160). Both presented positive serology (IgG) for Toxoplasma gondii. A control group (G3: n = 160) with patients with negative serology was included. The characterization of the CCR5∆32 and CCR5 59029 A/G polymorphisms was done by PCR and PCR-RFLP, respectively. The PCR products were analyzed by agarose gel electrophoresis.

Results: The difference between the groups in respect to the mean age was statistically significant (G1 vs G2: p<0.0001; t = 7.21; DF = 318; G1 vs G3: p<0.0001; t = 4.32; DF = 318; G2 vs G3: p<0.0001; t = 9.62; DF = 318). There were statistically significant differences for the CCR5/CCR5 genotype (p = 0.008; OR = 0.261; CI = 0.74 – 0.95) in comparison to G2 group. The genotypes AA (p = 0.007; OR = 2.974; CI = 1.39 – 11.44) and AG (p = 0.018; OR = 2.447; CI = 1.36 – 11.70) also presented differences statistically significant between G1 and G2 groups. The Nagelkerke $r^2$ value was 0.040 or 4%.

Conclusion: Individuals with the CCR5/CCR5 genotype and simultaneously the CCR5 59029 AA or AG genotypes have a great risk to develop ocular toxoplasmosis, which may be associated with strong and persistent inflammatory response in the ocular tissue.
Diagnostic accuracy of recombinant BP26 (outer membrane protein 28) of Brucella melitensis for enzyme-linked immunosorbent assay of human brucellosis

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Background: Brucellosis is a zoonotic disease in humans and animals with worldwide distribution and was known as an endemic disease in Iran. Early and accurate diagnosis of brucellosis needs to an accurate laboratory method. The aim of this study was to assess the accuracy of assay indirect Enzyme-linked immunosorbent assay (ELISA) for the detection of brucellosis in humans in order to have an appropriate alternative to conventional tests such as Wright, 2ME, and commercial ELISA kits.

Methods & Materials: In this study, common strains of Brucella in Iran isolated and Bp26 gene amplified and produced. Then by using PET vector transferred into bacteria Bl21. Recombinant protein Bp26 produced and after confirmation by SDS-PAGE and Western blot, tests were used as the antigen to cover the microplate. 124 serum samples included 62 normal healthy individuals and 62 patients with acute brucellosis that approved by STA and 2 ME tests were entered into the study. The results of this study by using SPSS (ver.18) were analyzed.

Results: Bp26 gene of obtained from brucella isolates, amplified and protein Bp26 expressed and purified. The sensitivity of 92% and specificity of 87% and positive predictive value of 88% and negative predictive value of 92% and accuracy 90% respectively were determined.

Conclusion: This kit with relatively good accuracy, sensitivity and specificity can be a good alternative to commercial ELISA kits.
Point-of-Care Molecular Diagnosis of Cutaneous Leishmaniasis and Intercurrent Fungal and Mycobacterial Infections
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Background: Due to the highly toxic nature of standard drugs used in the treatment of cutaneous leishmaniasis (CL), and overlapping clinical features of CL with ulcers due to fungal and mycobacterial infections, confirmatory diagnostic testing must be undertaken. We evaluated the performance characteristics of a handheld battery operated device for differentiation of Leishmania from known fungal and mycobacterial causes of cutaneous ulcers.

Methods & Materials: Using ATCC strains of Leishmania (L. V. braziliensis, L. V. panamensis, L. V. guyanensis), mycobacteria (M. abscessus complex) and fungi (Paracoccidioides brasiliensis), we validated PalmPCR for detection of Leishmania, fungal, and mycobacterial species known to cause cutaneous ulcers. We further validated the device for detection of Leishmania from clinical specimens including filter paper lesion impressions, cytology brushes, and tissue. Respective primers targeted a conserved region of kinetoplast DNA (kDNA) for detection of Leishmania, pan-mycobacterial Hsp65, and pan-fungal ITS3/4 regions. PCR products were visualized using the EGel Go reader, a portable battery-operated system for agarose electrophoresis. Outcome measures were sensitivity and specificity, where conventional end-point or real time PCR was the reference standard.

Results: Compared to the reference standard, the PalmPCR device detected 100% of ATCC strains of Leishmania, fungi, and mycobacteria. There was no cross-reactivity of primers with any negative control. The PalmPCR device accurately categorized reference specimens as positive or negative for Leishmania 91.3% of the time (42/46 specimens), yielding sensitivity and specificity of 90% and 91.7%, respectively. Sensitivity of point-of-care PalmPCR for detection of Leishmania in a clinical field setting enrolling patients with suspected CL was 100% compared to reference real time PCR. In 56% of field patients with CL, pan-mycobacterial and/or pan-fungal primers detected co-colonization with species such as Malassezia spp., Aspergillus spp., and Cladosporium spp. In one patient with CL, Mycobacterium doricum was also detected in the ulcer.

Conclusion: We have verified that the PalmPCR device performs comparably to conventional end-point or real time PCR for the detection of Leishmania, fungi, and mycobacteria. This work has implications for CL diagnostic process improvement, and has the potential to improve point-of-care diagnostic sensitivity compared to conventional tests such as smear.
Risk Assessment across the Event Continuum: a Canadian Approach for Emerging and Endemic Zoonotic Diseases

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Background: Emerging and endemic zoonotic disease (ZD) events (e.g. outbreaks) are identified and communicated regularly to public health. A systematic approach is needed to assess the risks associated with these events and inform decision making across the event continuum, from first detection to completion of response activities.

Methods & Materials: Expert panels were created focusing on 1) initial threat assessment, and 2) more in-depth “rapid” risk assessment. For initial threat assessment, multi-criteria decision analysis (MCDA) tools and decision-tree methods were reviewed, adapted, and tested by the expert panel, focusing on the ability to promptly generate clear concise evidence-based risk statements. The tool was assessed after a month-long pilot with key user and stakeholder interviews. For more in-depth risk assessment, the group identified two desired output products: a quick “Situation Assessment” and a more in-depth “Rapid Risk Assessment”. Microsoft Excel was used to design the modules supporting a common approach for the identification and documentation of populations at risk, likelihood of infection, and impact.

Results: Two tools were designed: 1) for initial threat assessment, the TSEID (Threat Scoring Tool for Emerging Infectious Diseases) was completed and tested, and 2) for rapid risk assessment, the RAIDER (Risk Assessment for Infectious Disease Event Response) is currently in development. The format of the TSEID is a decision-tree MCDA flow-chart and user guide with definitions. Results from the pilot suggested that the TSEID enabled timely ranking of events, helped create risk statements that highlighted attributes of concern, with overall positive results on use and utility from users and stakeholders. The RAIDER is being designed to support more in-depth rapid risk assessment, with modules including flow-charts/decision trees, risk questions, a quantitative module that links the assessment to models and relevant data, and an audit trail. Initial assessments suggest it will be useful for defining populations, assigning risks (likelihood and impact) and documenting rationale.

Conclusion: The TSEID and RAIDER were designed to improve the risk assessment process for ZD events affecting Canadians in Canada and abroad. Both tools rely on systematic and transparent methods, enabling the production of standardized reports for decision makers. Preliminary assessments of the tools have been promising.
Leptospira Epidemiology in dairy cattle in Bangladesh
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Background: Bovine Leptospirosis causes enormous economic loss due to reproduction and production loss. It has been perceived as a rising global public health issue. Spirochetes with various pathogenic types of the family Leptospiraceae have zoonotic significance. Bovine species acts as career or vectors, whereas human are the dead end host. No scientific attempt has previously been taken to investigate epidemiological diversity of Leptospira in commercial dairy cattle in Bangladesh. Hence, a cross-sectional study was conducted in commercial dairy cattle in Bangladesh to describe epidemiological scenario of Leptospira (Leptospira prevalence, Leptospira antibody prevalence and associated risk factors).

Methods & Materials: Nineteen upazillas from 12 districts of 7 divisions were randomly chosen for the study. A total 43 dairy cattle farms were recruited based on the presence of abortion history within past six months. Pretested questionnaire was used to collect epidemiological information. Blood and urine samples and aborted fetuses were collected for laboratory evaluation. Sero–positivity for Leptospirahardjo was evaluated on ELISA technique. Dark Field Microscopic examination was farmed on urine samples. Aborted fetus was evaluated through bacteriological culturing followed by PCR. The PCR positive samples were further sequenced for phylogenetic analysis. Statistical analysis was carried out on field and laboratory data as required by using STATA software.

Results: The overall sero – prevalence of Leptospira was 0.179 (95% CI: 0.094 - 0.314) in dairy cattle in Bangladesh. The proportionate Leptospira prevalence was 55.6 % in cattle and 32% in fetuses and 32% in specimens obtained from fetuses prevalence has been estimated from urine and fetal sample respectively. Breed (Exotic vs Cross: OR= 3.4), age (≥4.6 vs ≤4.5: OR=5.0) and parity (0-1 vs 2-3: OR=3.1) were identified as potential risk factors. The sequences of Leptospira in the present study (Cattle Bangladesh F/1-825) had a close congener (78%) of the sequence of Leptospira isolated from cattle in Brazil.

Conclusion: A substantial amount of Leptospirosis is present in the commercial cattle population of Bangladesh. Measures including rodent control, quarantine of the new animal as well as isolation and treatment of the diagnosed animal should be carried out.
Detection of Antibodies to Hydatid Infection in Cattle in Farms and at Slaughter in Kaduna, North-Western Nigeria

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Background: Hydatidosis caused by *Echinococcus granulosus* is a global animal and human health problem of increasing economic and public health importance. This study aimed at determining the prevalence of *E. granulosus* antibodies in cattle farms and at slaughter in abattoirs in Kaduna North-Western, Nigeria.

Methods & Materials: This was a cross-sectional study conducted in cattle slaughtered at the Tudun-Wada and Kawo abattoirs and seven cattle farms. A total of 700 samples comprising 350 samples each were collected from the farms and the abattoirs. The 700 sera were subjected to ELISA test. Postmortem inspection of the viscera of animals which blood were collected from was conducted at the abattoirs.

Results: The prevalence of *E. granulosus* antibodies by ELISA was 46.00% (161) and 4.57% (16) in the farms and at slaughter respectively. No obvious cysts were recovered during the postmortem inspection of the organs of the sampled slaughtered cattle. Prevalence of 20.00% was recorded in cattle < 2yr of age, 4.30% in 2-5yr and 4.49% in > 5yrs at slaughter while the prevalence of 75.00%, 44.40% and 49.43% were observed in age groups < 2yrs, 2-5yrs and > 5yrs respectively in the cattle farms. Antibodies to *E. granulosus* were observed in both male and female cattle at slaughter with prevalence rates of 5.44% and 3.44% respectively. There was no association (P = 0.4405) between *E. granulosus* antibodies and the sex of the cattle. Antibodies to *E. granulosus* were observed in both male and female cattle on the farms with prevalence rate of 43.75% and 46.67 % respectively. There was no significant difference (P=0.6457) in seroprevalence between the sexes. There was a statistically significant difference between the breeds in the cattle farms with seroprevalence of 40.73%, 57.61% and 70.00% in the indigenous, crosses and exotic breeds respectively. There was association (P=0.0065) between hydatid antibodies and the breed of cattle in the farms.

Conclusion: The detection of antibodies to hydatid infection is of great veterinary/public health importance, hence routine screening of cattle is of importance in order to prevent transmission to man.
Anti-feeding and insecticidal efficacy of Vectra 3D (dinotefuran, permethrin, pyriproxyfen) against Aedes aegypti mosquitoes in dogs over 8 weeks
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Background: To our knowledge, the efficacy of topical solutions against flying insects was never investigated beyond 1 month after administration. The aim of the current study was to assess the duration of efficacy of Vectra 3D (dinotefuran, permethrin, pyriproxyfen, DPP) against Aedes aegypti mosquitoes over 8 weeks.

Methods & Materials: Sixteen dogs were enrolled and allocated to 2 groups based on the pre-treatment feeding rate of mosquitoes: a control untreated group (n=8) and a DPP treated group (n=8). Treatment was administered on day 0 as a line-on at the minimum recommended dose (0.12 mL/kg BW). On days 1, 7, 14, 21, 28, 35, 42, 49 and 56, dogs were sedated and challenged with 80 unfed female mosquitoes for 60 min. The mosquitoes were classified as fed/unfed and live/moribund/dead. All the live and moribund mosquitoes were incubated for 24h and assessed for viability. Anti-feeding (repellency), knock-down and insecticidal efficacy of DPP was calculated using the Abbott formula.

Results: Feeding (62-87%) and viability (1h, 68-79%) of mosquitoes in the control group was high all along the study. At 24h after administration, the anti-feeding efficacy was already 88%, knock-down effect at the end of the 1h exposure was 92% and insecticidal efficacy was 78.4%. Most of the mosquitoes incubated from this first challenge did not survive (99.8%). Repellency of DPP remained >91% from day 7 to 28 and >80 % up to day 56. Knock-down effect within 1h of exposure was >52.3% and insecticidal efficacy (24h incubation) was > 92% from day 1 to 56.

Conclusion: The study confirms the rapid onset and demonstrates the long-lasting efficacy of Vectra 3D against mosquitoes that may carry various pathogens such as heartworm. In real-life situations, compliance is a recurrent issue and pet owners may not follow the monthly administration schedule. This dataset provides the evidence of the high efficacy standard of the product and additional piece of mind for the prescribing veterinarian.
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**Background:** Children are known to be the most vulnerable group in the world for rabies disease, however, little is known about their involvement in the post-exposure prophylaxis (PEP), including wound cleaning, vaccination, and rabies immunoglobulin administration. This study aims to explore this knowledge gap, by providing factors and possible mechanisms that can explain children’s involvement in the rabies post-exposure prophylaxis. This study was conducted in Bajawa district, Flores East Nusa Tenggara, Indonesia. At the time this study was conducted, Bajawa district was endemic for rabies disease.

**Methods & Materials:** Story telling interviews with 23 children (7-15 years) who had a dog bite experience and in-depth interviews with 20 of dog bite victim’s parents/caregivers have been conducted. Interviews were then analysed qualitatively using content analysis. Guided by COM-B model, Capabilities, Opportunities, and Motivations were explored.

**Results:** The findings suggest, when a dog bite exposure occurs in children, not only parents/caregivers but also children can influence the involvement of a necessary rabies PEP. Mainly, parents/caregivers conduct the initial phase of wound cleaning, direct vaccination-seeking behaviour, to its completion. Children, in the other hand, could affect greatly the success of PEP in the level of willingness to inform the accident to their parents/caregivers, to conduct the wound cleaning, and to complete the vaccination treatment. Some important factors which can hinder the necessary involvement of children in the rabies PEP are the perception of parents/caregivers and children that scratches from dogs are not a risk, the insecurity among children to report dog bites to their parents, the lack of knowledge and capability on wound cleaning, minimum operating-hours of the treatment facility, and low vaccine availability.

**Conclusion:** This study shows that public health practitioners in Bajawa district may need to involve both children and parents/caregivers in the control measure program of rabies, educate both of them to increase their knowledge and capacity about the proper treatment after dog exposure, and enlarge their opportunities to meet the treatment.
Antibiotic usage in dairy practices: potential role in emergence of antibiotic resistance

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**Background:** Antimicrobial resistance has emerged as one of the major health-related problem throughout the world with increased concern in developing countries like India. In the emergence of antibiotic resistance, animal husbandry practices play an important role in spreading resistant pathogens to humans. The non prudent use of antibiotics in dairy animals leads to occurrence of antibiotic residues in milk and hence further substantiates the emergence of resistant pathogens.

**Methods & Materials:** The present study aimed at detection of antibiotic residues in raw milk samples procured from 166 dairy farms located in one of the major milk producing state of India, Punjab. The dairy farms were categorized according to their herd size into small (less than 10 animals), medium (10-30 animals) and large (more than 30 animals) farms. A total of 492 samples (164 samples from each farm type) were analyzed using High Performance Liquid Chromatography (HPLC) for the presence of enrofloxacin, oxytetracycline, tetracycline, doxycycline, sulphamethoxazole, sulphadiazine and chloramphenicol residues.

**Results:** A total of 20 (12.1%), 31 (18.9%) and 27 (16.5%) samples were found positive for antibiotic residues from large, medium and small dairy farms, respectively. Five (3%), 7 (4.9%) and 8 (4.3%) samples from large, medium and small dairy farms, respectively were found above maximum residue limits established by European Union/Codex Alimentarius Commission. The samples were found positive for enrofloxacin, oxytetracycline, tetracycline and sulphamethoxazole residues but none of the sample was positive for doxycycline, sulphadiazine and chloramphenicol.

**Conclusion:** The occurrence of antibiotic residues in milk samples above maximum residue limits suggested possibility of unacceptable health risks to consumers. As milk containing antibiotics in sub-lethal concentrations when consumed for longer duration may substantiate emergence of antibiotic resistance in consumers, so strategies pertaining to judicious use of antibiotics in dairy practices should be implemented.
Live bird markets in Bangladesh as a potential source for Avian Influenza Virus transmission

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**Background:** Live bird markets (LBM) are crucial for trading poultry in many developing countries where they are being considered hotspots of Avian Influenza Virus (AIV) prevalence and contamination.

**Methods & Materials:** An active surveillance for Avian Influenza Virus (AIV) was conducted on four species of LBM birds (chickens, ducks, quails and pigeons) from 10 of the largest LBM in Chittagong, Bangladesh, and two species of peri-domestic wild birds (house crow and Asian pied starling) in their direct vicinity from November 2012 until September 2016. Our aim was to identify the scale and annual pattern of AIV circulation in both the LBM birds and the two wild bird species living in close proximity of the LBM. In the latter two species the annual pattern in AIV antibody prevalence was additionally investigated. A total of 4770 LBM birds and 1119 peri-domestic wild birds were sampled. We used rt-PCR for detection of the AIV M-gene and AIV subtypes H5, H7 and H9 from swab samples. We used c-ELISA for AIV antibody detection from serum samples of wild birds.

**Results:** Average AIV prevalence among the four LBM species varied between 16 and 28%, whereas no AIV was detected in wild birds. In all LBM species we found significantly higher AIV prevalence in winter compared to summer. A similar pattern was found in AIV antibody prevalence in wild birds feeding in the direct vicinity of LBM. For the subtypes of AIV investigated, we found a significantly higher proportion of AIV H5 in LBM chickens and H9 in LBM ducks. But no H7 was detected. We conclude that AIV and notably AIV H5 and H9 were circulating in the investigated LBM of Bangladesh with clear seasonality that matched the prevalence of AIV antibodies of peri-domestic wildbirds.

**Conclusion:** Our data suggest considerable exchange of AIV within and among the four LBM bird species and wild birds, which likely contributes to the maintenance of the AIV problems in Bangladesh. Increasing biosecurity and notably reducing the direct and indirect mixing of various domestic bird species and wild birds with regular use of disinfectant are likely to reduce the risk of transmission of AIV, including HPAI.
Signatures of memory immunity in long recovered Sudan virus survivors sheds light on the role of individual viral proteins in triggering memory immune activation

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**Background:** Survival from ebolavirus correlates with balanced, specific, adaptive immunity and distinct immune signatures are observed upon recovery. Immune mediators of survival, during acute and early convalescent stages, have been determined, however the comprehensive profile of antigen specific memory immunity, mediating long term protection have yet to be defined

**Methods & Materials:** To address this, we examined residual cellular and humoral immune responses in long-recovered survivors (>10 years post infection) of the Sudan virus (SUDV) outbreak in Gulu, Uganda (2000–2001) against SUDV and four SUDV recombinant proteins, the glycoprotein (GP\(_{1-649}\)), nucleoprotein (NP), and viral proteins 30 (VP30) and 40 (VP40). Cytokine and chemokine expression levels in SUDV PBMC cultures were assessed by multiplex ELISA and flow cytometry following specific SUDV viral protein and irradiated whole virus stimulation. Antibody corresponding neutralization titers and ADCC capacity were also determined.

**Results:** Flow cytometry and multiplex ELISA results from SUDV survivors demonstrated significantly elevated levels of antigen specific Th1 cellular response following NP stimulation, which correlated with high titers of IgG antibodies and serological neutralizing activity. These survivors also demonstrated the capacity to strongly mediate an ADCC response through the FcγRI reporter with antibodies directed to GP\(_{1-649}\).

**Conclusion:** This previously undefined relationship between memory CD4 T cell responses and serological neutralizing capacity in SUDV survivors is key for understanding long lasting immunity, and correlates of protection in survivors of filovirus infections.
Awareness, Perception and Preferences of Mothers towards Mobile Phone Reminders for Routine Childhood Immunization Appointments in Ahmadu Bello University Teaching Hospital Shika, Zaria, Nigeria

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Background: Adherence to childhood immunization schedules is a function of various factors. Given the increased use of technology as a strategy to increase immunization coverage, the aim of the study was to determine the awareness, perception and preferences of mothers towards mobile phone reminders for routine childhood immunization appointments in Ahmadu Bello university teaching hospital, Shika, Zaria.

Methods & Materials: A cross-sectional descriptive study among 300 mothers’/care givers attending routine childhood immunization clinic in ABUTH Shika were selected using systematic random sampling technique. Data was collected using the Open Data Kit (ODK), which sought information on socio-demographic characteristics, awareness, perception and preferences of mothers towards mobile phone reminders for routine childhood immunization appointments, and data was analyzed using SPSS version 21 and results were presented in tables and charts. Relationship between categorical variables were assessed using Chi Square test at P < 0.05.

Results: Most of the respondents were within the age group 25-29 years (27.3.0%) years, with a mean age of 28.66, employed,(49.3%) and had secondary school education (42.7%). Majority of the respondents had mobile phones (78.3%), 96.3% had good perception and only 23.3. % had ever heard of RI reminder. However, 86.0% were willing to give their cell phone numbers in the clinics for RI reminder, 83.7% were willing to receive and 72.5% were willing to pay for RI reminder. The preferred communication modes were cell phone calls (77.7%) or text messages/SMS (70.9%), and 16.3% were not willing to receive any form of RI reminder. There was significant statistical relationship between educational status, socioeconomic status, and phone ownership of mothers with being aware of RI reminder.

Conclusion: The respondents had good perception, but lack awareness, on immunization reminder and they prefer phone call and SMS for childhood RI reminder, therefore the need for public awareness on use of mobile phones for RI reminder and recording of mobile phone numbers during Antenatal visits.
Oral immunization of a rAd vector expressing norovirus VP1 elicits a potent mucosal immune response without an increase in anti-vector immunity

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Background: Noroviruses are the leading cause of epidemic acute gastroenteritis and foodborne diarrheal disease in humans. Potential correlates of protection identified through human challenge studies include mucosal IgA, memory B cells, and serum blocking (BT50) antibody titers. We hypothesized that fecal and memory IgA responses would be significantly elevated following oral immunization.

Methods & Materials: We conducted a single-site, randomized, double-blind, placebo-controlled trial to determine the safety and immunogenicity of a norovirus vaccine consisting of a non-replicating adenovirus vector expressing VP1 delivered orally by tablet. Subjects that met inclusion/exclusion criteria were enrolled and randomized 2:1 to receive either a single dose of vaccine or placebo, respectively. Two dose levels were evaluated. The primary objective was to assess safety. The secondary objective was to determine immunogenicity, primarily assessed by measuring serum BT50. Exploratory immunological assessments included serum, fecal and saliva antibody titers measured by and the frequency of memory and antibody secreting B cells (ASCs). Anti-vector immunity was assessed by measuring Ad5 neutralizing antibody responses pre and post immunization (ClinicalTrials.gov number NCT02868073).

Results: Sixty-six subjects were enrolled between July and Sept 2016. The vaccine was well-tolerated. The primary immunological endpoint (BT50 titers) was met in low and high dose groups (P=0.0014, P<0.0001). In the high-dose group, 18/23 (78%) subjects had a two-fold or greater increase in BT50 titer after a single vaccine dose. An average of 561 IgA ASCs x10^6 PBMC were induced post-immunization in the high dose group. Post immunization, a 15 fold increase in the geometric mean was observed, along with a greater than 10 fold average increase in the fecal IgA VP1 specific antibody response. Anti-Ad5 neutralizing antibody responses did not significantly increased compared to the placebo group.

Conclusion: The norovirus vaccine was well-tolerated (with no dose limiting toxicities), and generated immune responses to norovirus VP1, without a corresponding increase in anti-Ad5 neutralizing antibody responses. In particular, the vaccine generated memory and local effector IgA+ B cells. Because mucosal IgA is the front-line defense against enteric pathogens, vaccine-derived norovirus-specific intestinal IgA may translate to superior efficacy. This is a very promising advance in the development of an oral norovirus vaccine.
Protection from homologous influenza challenge in humans after oral immunization of a rAd vector expressing HA

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Background: Influenza vaccines are recommended for all age groups (6 months and older) in the US, but vaccine uptake in 18-49 year-old adults in 2016-2017 was estimated to be only 32% (CDC). An oral tablet delivered to the work place or mailed to home might improve vaccine uptake. We tested the ability of an oral tablet to protect against illness in an influenza human challenge study.

Methods & Materials: We conducted a single-site, randomized, double-blind, placebo-controlled trial of an influenza vaccine to determine the safety, immunogenicity and efficacy of a non-replicating adenovirus vaccine expressing HA delivered by tablet. Subjects were prescreened to have low HAI titers. Those that met inclusion/exclusion criteria were enrolled and randomized 2:2:1 to receive either a single dose of oral tablet vaccine, QIV, or placebo, respectively. The primary objective was to measure efficacy, determined by homologous challenge three months post-immunization. The efficacy was measured primarily by illness, a combination of shedding (qRT-PCR) plus symptoms on the Flu-Pro questionnaire.

(ClinicalTrials.gov number NCT02918006).

Results: Over 10,000 subjects were screened to identify subjects with low HAI titers (< 1:10) to A/CA/07/2009. 179 subjects were immunized, and 3 months post-immunization, 143 subjects completed the challenge phase in 6 cohorts. The oral tablet vaccine group was protected against illness in 70.7% (41/58) of subjects, versus 64.8% (35/54) in QIV subjects, versus 51.6% (16/31) in placebo subjects. Both vaccines significantly reduced the probability of shedding relative to placebo (Bayesian posterior p<0.01). The immunological correlate of protection from illness for the oral vaccine was the ability to generate an IgA ASC response (p=0.0005 in a logistic model fit), whereas for the QIV group protection was found to correlate more tightly with HAI titers.

Conclusion: The oral vaccine may open up new markets for an influenza vaccine, particularly for the working adult population. Further, with a potential different immunological profile than an injected inactivated vaccine, the oral vaccine tablet may be able to provide enhanced protection in those people that already have a circulating neutralizing antibody response to influenza.
Surface engineered vesicular carriers for transmucosal immunization via the nasal route
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**Background:** The critical role of vaccine delivery system in “rational vaccine design” has been widely recognized. Thus research work was envisaged involving development of IgG antibody immobilized on the surface of hepatitis B surface antigen (HBsAg) antigen–loaded liposomes. which offered increased uptake of nanoliposome through transmucosal surface of nasal route and sustaining release of HBsAg to evoke relatively high IgA titre in mucosal surface.

**Methods & Materials:** Liposomes were prepared by a lipid cast film method & then IgG antibody was crosslinked on the surface. Coated liposomes were characterized in-vitro for their shape, size, polydispersity index, entrapment efficiency, zeta potential and stability. Fluorescence microscopy was performed to confirm the deposition pattern in respiratory tract. The in-vivo part of the study was conducted to visualize targeting potential, localization pattern, and immunogenicity. In addition, immune response was compared with alum-HBsAg vaccine injected intramuscularly.

**Results:** Observation of fluorescence images of nasal mucosa, lungs and spleen, revealed that these antibody coated liposome, were significantly taken up by mice respiratory mucosal surface, which made them promising carriers for mucosal vaccination. Considerable immune responses were produced by the developed system that may be due to the induction of MALT as well as contribution of the peripheral airways.

The serum anti-HBsAg titer, obtained from the postnasal administration of IgG-coupled liposomes, was significantly higher than plain liposomes. Moreover, IgG-coupled liposomes generated both humoral (i.e., systemic and mucosal) and cellular immune responses upon nasal administration, while the alum-adsorbed antigen displayed neither cellular (cytokine level) nor mucosal (IgA) response. The formulation also displayed enhanced transmucosal transport, improved in-vitro stability, and effective immunoadjuvant property.

**Conclusion:** The higher immunity induced by ACL HBsAg may be attributed to its cationic nature, antibody coating and subsequent mucoadhesive property. Thus mucosal immunization with lipid vesicle through nasal administration may be effective in prophylaxis of diseases transmitted through mucosal routes as well as systemic infections. The strategy can be made more appropriate by determination of paracellular transport, nasal mucociliary clearance, mucosal toxicity assessment etc.