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Dong Hoon Suh, Crit Care Obst & Gyne 2018, Volume: 4
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HOXB9 AS A POTENTIAL TARGET GENE FOR OVERCOMING PLATINUM RESISTANCE IN MUCINOUS OVARIAN CANCER

Dong Hoon Suh
Seoul National University Bundang Hospital, Korea

Although ovarian cancer is heterogeneous with various histologic types, current treatment guidelines are generally the same for all histologic types. Expression of HOX genes in epithelial ovarian cancer (EOC) was known to be histology-specific. We performed a series of in vitro and in vivo studies to find out a tailored strategy of inhibiting HOXB9 expression for overcoming platinum resistance in mucinous EOC. HOXA10 and HOXB9 showed exclusively high expression in SKOV-3 and RMUG-S, respectively. HOXA10 siRNA treatment made a significant decrease in cell viability of SKOV-3, but not RMUG-S. By contrast, HOXB9 siRNA treatment made a significant decrease in cell viability of RMUG-S, but not SKOV-3. HOXA10 siRNA and HOXB9 siRNA treatments: increased the expression level of cleaved PARP and caspase-3 in SKOV-3 and RMUG-S, respectively; expression of vimentin was decreased while expression of E-cadherin was increased; SOX-2, Nanog, and Oct-4 also decreased in both cell lines after specific siRNA treatment. When injected with RMUG-Sko HOXB9 and SKOV-3oe HOXB9 in mouse models, we clearly showed that the tumours from RMUG-Sko HOXB9 grew significantly slower than those from control. By contrast, the tumours from SKOV-3oe HOXB9 grew significantly faster than those from control. After harvesting, the cells from the SKOV-3oe HOXB9 were characterized with resistance to cisplatin and higher expression of vimentin than those form the control. Our findings suggest that platinum-resistance of mucinous ovarian cancer might be defeated by inhibiting HOXB9, which could be a target of tailored strategy for overcoming the resistance to platinum in mucinous EOC.

Biography

Dong Hoon Suh is a Clinical Professor of the Department of Obstetrics and Gynaecology in Seoul National University Hospital. He is a Gynaecologic Oncology Specialist. He has graduated from Seoul National University School of Medicine at 2002 and completed his PhD at the same university, postgraduate school in 2014. He has published more than 50 papers in reputed journals of his field. He is a Vice Secretary General of organizing committee of the Asian Society of Gynecologic Oncology (ASGO) and a Principal Editor of its official journal, Journal of Gynecologic Oncology. He has been also deeply involved in other medical journal activities as a Committee Member for Planning and Evaluation of Korean Association of Medical Journal Editors, KAMJE.

sdhwcj@naver.com

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BOTTLENECKS TO UNIVERSAL IMMUNIZATION COVERAGE IN AFRICA

Edison Arwanire Mworozi and Joseph Rujumba
Makerere University, Uganda

Vaccination is a cornerstone of any program that aims at reducing morbidity and mortality due to preventable infectious diseases and is a cost-effective intervention. Despite efforts to reduce child mortality, 10 million children under 5 die annually mainly from developing countries, Africa inclusive. It is estimated that currently Africa contributes to over 50% of the global childhood deaths due to vaccine preventable diseases. Vaccine preventable diseases remain an important public health problem. Immunization is a key in attaining sustainable development goal 3 i.e. reducing under-five mortality globally but attaining universal childhood vaccination remains a challenge particularly in reaching the most vulnerable in Africa. Despite the availability of effective vaccines, immunization coverage remains low in most parts of Africa due to various bottlenecks including: inadequate and poorly motivated health workers (HWS), inadequate knowledge and skills by HWS, multiple languages, low education, cultural and religious beliefs, poor access to heaths facilities, social economic status, political instability, conflicts and social unrest, ever increasing refuges or internally displaced persons, mobile populations, inaccurate population and immunization data, negative messaging and anti-vaccine lobby, inadequate funding, social mobilization and vaccine safety concerns. These bottlenecks have led to minimal improvement or stagnation in immunization coverage rates in recent years in a number of African countries threatening to reverse the gains achieved in the past two decades. Achieving universal immunization coverage in Africa remains a daunting task, requires multiple strategies and partnerships.

Biography

A Ugandan Pediatrician with keen interest in infectious diseases and childhood immunization. Currently, he a Senior Consultant Pediatrician at Mulago National Referral Hospital, Honorary Lecturer at the College of Health Sciences Makerere University and Professor of Pediatrics, St Augustine Internal University Actively involved in the Uganda National Expanded Programme on Immunization and introduction of New Vaccines into routine immunization. He has published widely and a Peer Reviewer for several journals. A member of several professional and technical bodies including: the Uganda Medical association, Uganda Pediatric Association, International Society for Infectious diseases, International Pediatric Association, Vienna Vaccine safety Initiative, East African Rotavirus Advisory Board (GSK) and Institutional Biosafety committees for the Makerere University and Walter Reed Collaborative HIV Vaccine Trials; East African Centre for Vaccines and Immunization; External Expert Advisory group on Stronger Systems for Routine Immunization Project in Uganda and a Member of the East African Meningococcal Advisory Board (Pfizer).

emworozi@gmail.com

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SURVIVAL OUTCOMES OF ADJUVANT THERAPY IN UTERINE-CONFINED ENDOMETRIAL CANCER WHICH HAS SEROUS PAPILLARY AND CLEAR CELL HISTOLOGY: RADIOTHERAPY VERSUS CHEMOTHERAPY

Miseon Kim[1], Byung Su Kwon[2], Ha Kyun Chang[3], Seungmee Lee[4], Suk-Joon Chang[5], Jin Young Choi[6], Sang-Yoon Park[3], Maria Lee[7], Hee-Sug Ryu[5] and Yong Beom Kim[8]

[1]CHA Gangnam Medical Center, CHA University School of Medicine, Republic of Korea
[2]Pusan National University Hospital, Republic of Korea
[3]Center for Uterine Cancer-National Cancer Center, Goyang, Republic of Korea
[4]Keimyung University, Republic of Korea
[5]Ajou University, Republic of Korea
[6]Chungbuk National University Hospital, Republic of Korea
[7]Seoul National University, Republic of Korea
[8]Seoul National University Bundang Hospital, Republic of Korea

Objective: To evaluate the survival outcomes of adjuvant therapy in uterine-confined endometrial cancer with serous papillary and clear cell histology

Methods: Medical records of 80 women who underwent surgical staging including hysterectomy and bilateral salpingo-oophorectomy between Nov' 2004 and Dec' 2017 were retrospectively reviewed. All study population was pathologically diagnosed as serous papillary and clear cell endometrial carcinoma confined to uterus after surgery. Survival outcomes were calculated by Kaplan-Meier method and compared using log-rank test between the women received radiotherapy and chemotherapy.

Results: 54 (67.5%) and 26 (32.5%) women were confirmed as serous papillary and clear cell histology after surgery, respectively. Adjuvant therapy was performed in 59/80 (73.8%) women: 25 of radiotherapy and 34 of chemotherapy. High level of preoperative serum CA-125 (25.1±20.2 vs. 11.5±6.5 IU/mL, p<0.001), open surgery (42 (71.2%) vs. 6 (28.6%), p=0.001), myometrium invasion >1/2 (20 (33.9%) vs. 0, p=0.002) and lymphovascular space invasion (LVSI (lymphovascular space invasion), 17 (28.8%) vs. 1 (4.8%), p=0.023) were frequent in the women with adjuvant therapy. However, pathological results including histology type, myometrial invasion ≥1/2 and LVSI were not different between the women received radiotherapy and chemotherapy. Five-year progression-free survival (78.9 vs. 80.1%, p>0.999) and overall survival (77.5 vs. 87.8%, p=0.373) were also similar in the two groups. Neither radiotherapy (Hazard ratio (HR) 1.810, 95% confidence interval (CI) 0.297-11.027; p=0.520) nor chemotherapy (HR 1.638, 95% CI 0.288-9.321; p=0.578) was independent associated factor for disease recurrence in multivariate analysis.

Conclusion: Our findings show that radiotherapy and chemotherapy have similar survival outcomes in uterine-confined endometrial cancer with serous papillary and clear cell histology. Further study with stratified analysis by myometrial invasion or LVSI was required.

shemme@naver.com
miseonkim@chamc.co.kr

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AN IN VITRO HUMAN CELL CULTURE MODEL OF NALT TO EVALUATE HUMORAL IMMUNE RESPONSE TO INFLUENZA VACCINES

Waleed Mahallawi[1,2] and Qibo Zhang[2]

[1]Taibah University, Saudi Arabia
[2]University of Liverpool, UK

Background: Influenza is a mucosal infection in the respiratory tract which is transmitted through the nasal mucosa. Human adenoids and tonsils are major components of local mucosal immune organs namely; nasal-associated lymphoid tissue (NALT) in humans and are known to be important induction sites for both mucosal and systemic immunity against upper respiratory tract pathogens. In this study, an in vitro cell culture model was used to describe the B cell immune responses induced by influenza vaccines.

Objectives: Human NALT derived immune cells is an important model to study immune response. Using NALT to measure immune response against influenza viruses is mimicking the natural immunity against the viruses.

Results: Intranasal live attenuated influenza virus-LAIV (FluMist) vaccine stimulation of NALT mononuclear cells (MNCs) induced IgG, IgA and IgM antibodies to pH1N1, sH1N1, and sH3N2. Additionally, flu vaccines also induced mucosal cross-reactive antibodies to aH5N1 following MNCs stimulation.

Conclusion: It is very important to use the human models to assess pathogens that causing human health problems such as influenza viruses. This model is very successful in terms of representing the natural infection.

Biography

He is currently working as a assistant professor in Taibah University, Saudi Arabia.

wmahallawi@gmail.com

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POULTRY VACCINES AND VACCINATION PRACTICES AMONG FARMERS IN WUKARI, TARABA STATE NIGERIA

Gbeminiyi R Otolorin[1], Olaolu T Olufemi[1], Danladi Tsokwa[2], Asabe A Dzikwi Emennaa[1], Solomon N Karshima[1], Hassana I Dunka[1], Eyiojo B T Baba-Onoja[2] and Ifeanyi E Edeh[2]

[1]University of Jos, Nigeria
[2]Federal University Wukari, Nigeria

Poultry enterprise is increasingly gaining viability owning to successful preventive measures of vaccination protocols for various diseases of economic importance. A cross-sectional study involving 45 poultry farms across the 6 wards in Wukari, local government area, Taraba State Nigeria; were surveyed to determine the vaccination practices and the vaccines used by poultry farmers. Purposive sampling was employed by Interviewer administered structured questionnaires in the course of the study. Fisher's exact test was used to test for association between categorical variables. A total of 8 (17.8%), 3 (6.7%), 3 (6.7%), 8 (17.8%), 6 (13.3%) and 17 (37.8%) farms were visited in Avyi, Bantaje, Chonku, Hospital, Jibu and Puje wards respectively. The 45 respondents were 57.8% male and 42.2% female farmers. A total of 26.7%, 40% and 33.3% fell within the age categories; 19-29 years, 30-39 years and ≥40 years respectively. Majority of the respondents never administered Marek's (82.2%), LaSota (51.1%), Komarov (75.6%), fowl cholera (75.6%) fowl typhoid (73.3%) and coccidiosis (68.9%) vaccines. Only 42.2% of the respondents had vaccination records while 51.1% had vaccination schedules. There was a significant association between disease outbreak and the use of infectious bursal disease, fowl typhoid, fowlpox and coccidiosis vaccines respectively. The association between the handling of vaccines and disease outbreaks were significant ($p<0.05$) for Marek's, infectious bursal disease, fowl typhoid and coccidiosis. The result of the association between vaccine administration against vaccine failures was significantly different ($p<0.05$) in all vaccines used. In conclusion, poultry farmers in Wukari are aware of routine vaccinations although a majority of them do not administer the vaccines and the few that use these vaccines have poor record and storage practices.

Biography

He is currently working as a faculty of veterinary medicine in university of Jos, Plateau State, Nigeria.

drniyiotolorin@yahoo.com

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HEPATITIS C VIRUS TESTING AND TREATMENT AMONG PERSONS RECEIVING BUPRENORPHINE IN AN OFFICE -BASED PROGRAM FOR OPIOID USE DISORDER IN NIGERIA

Adeyemi A Abati, Omosola A Akinbade, Samuel A Ayoola
Lagos University, Nigeria

Aims: In Nigeria, hepatitis c virus (HCV) infection is primarily spread through injection drug use. there is an urgent need to improve access to care for HCV among persons with opioid use disorders who inject drugs. the purpose of our study was to determine the prevalence of HCV, patient characteristics, and receipt of appropriate care in a sample of patients treated with buprenorphine for their opioid use disorders in a primary care setting.

Methods: This study used retrospective clinical data from the electronic medical record. the study population included patients receiving buprenorphine in the office based opioid treatment (obot) clinic within the adult primary medicine clinic at Lagos medical centre between October 2008 and august 2015 who received a conclusive HCV antibody AB test within a year of clinic entry. we compared characteristics by HCV serostatus using Pearson's chi-square and provided numbers/percentages receiving appropriate care.

Results: The sample comprised 300 patients. slightly less than half of all patients (n = 134, 27.7%) were HCV AB positive, and were significantly more likely to be older Hausas and Yoruba's, have diagnoses of post- traumatic stress disorder (ptsd) and bipolar disorder, have prior heroin or cocaine use, and be hi v- infected. among the 134hcvab positive patients, 126 (67.7%) had detectable HCV ribonucleic acid (rna)indicating chronic HCV infection; only 8 patients (2.21%) with chronic HCV infection ever initiated treatment.

Conclusions: Nearly half of patients (47.7%) receiving office-based treatment with buprenorphine for their opioid use disorder had a positive hepatitis c virus antibody screening test, although initiation of HCV treatment was nearly non- existent (2.21%).

abati_adeyemi@yahoo.com

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ADAPTATION OF LOCAL RABIES VIRUS ISOLATES TO HIGH GROWTH TITER AND PATHOGENICITY STUDY TO DEVELOP VACCINAL STRAIN IN ETHIOPIA

Abebe Mengesha Aga[1], Birhanu Hurisa[1], Tihitina Tesfaye[1], Hailu Lemma[1], Gashaw G/Wold[1], Amha Kebede[1], Tsehaynesh Mesele[1], Denis Bankovisky[2] and Kelbessa Urga[1]

[1]Ethiopian Public Health Institute, Addis Ababa, Ethiopia
[2]Pokrov Plant of Biologics, Russian Federation, Russia

Background: Rabies is a zoonotic viral disease which causes acute encephalitis in humans and animals. The case is most severe in developing countries where cell culture derived anti-rabies vaccines are unaffordable or the available nervous tissue-derived vaccines are of questionable immunogenicity and may cause neurological complications. The aim of this study was to adapt local rabies virus isolates on cell lines and mice brain and to study pathogenicity to intramuscular route of inoculation to develop vaccine strain locally.

Materials & Methods: The viruses were isolated from rabies dogs' brain and human saliva and adapted to Swiss albino mice brain and cell lines (BHK-21 and Vero) by several blind passages to increase viral titer. The viral titers were controlled by titration at each blind passage both *in vivo* and *in vitro*. For pathogenicity study, mice were inoculated intramuscularly with 250MICLD50/0.1 ml of each adapted virus isolates and observed for 45 days.

Results: By titration, a minimum of $10^{6.5}$ TCID50/ml (*in vitro*) and $10^{4.5}$ MICLD50/0.03 ml (*in vivo*) virus titer were obtained. According to pathogenicity study, only two virus isolates, human origin sululta (HOS) and dog origin (DO) caused 12.5% death.

Conclusion: Increase in viral titer was significant and it is observed for high viral titer by *in vitro* virus propagation. Death due to intramuscular inoculation can indicate the phylogroup origin of the viruses showing decline in virulence due to several blind passages. Adaptation of the viruses to mice brain and cell lines to increase virus infectivity titer significantly affects viral virulence to intramuscular inoculation. Further, genetic relationship with fixed rabies virus strain need to be studied by molecular techniques and vaccinal strain should be used from locally isolated viruses.

agagurmu@yahoo.com

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SITUATION CASE ANALYSIS OF DIPHTHERIA IN JAKARTA

Adrian Verry[1], Inggariwati, H Laili Nur, E Etrina and Widyastuti

[1]Jakarta Provincial Department of Health, Indonesia

Diphtheria is an infectious disease caused by infections of *Corynebacterium diphtheriae*. Diphtheria is still endemic in Indonesia with 342 cases reported in 2016 just lower than India and Madagascar with 3380 and 2865 cases respectively. In 2017, a surge of diphtheria cases happened in the country with 591 cases reported from Jan' to Nov' across 20 provinces and 95 districts. Jakarta is one of the provinces undergoing the surge of diphtheria cases. During the period of 2014-2016, there were only 31 reported cases in Jakarta province. Until the end of 2017, there were 120 reported cases of diphtheria with 17 of them were laboratory confirmed. There were 23 new cases reported since the turn of the year until the end of the first week of Feb' 2018. We found that the disease spread across the 5 out of 6 districts (only Thousand Island district reporting zero cases), and 39 out of 44 sub-districts. The disease affected people of all ages with children in the 5-10 year old age group and adults in 19-40 year old group have contributed the majority of the cases with 43 and 39 cases respectively. Overall, there is no significant difference in total number of cases between men and women. The majority of the cases (45%) were found to have received complete basic three-course of DPT immunization during their first year of life even though the proportion of those with unknown basic immunization status is also quite high (39%). The proportion of cases who received booster vaccination is 12%. 22% of the cases did not receive any booster vaccination while the other 66% have unknown booster vaccination status.

dr.verry@gmail.com

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ASSESSMENT OF VACCINE WASTAGE IN THE UNIVERSAL IMMUNIZATION AND PULSE POLIO IMMUNIZATION PROGRAMS OF INDIA

Ajit Mukherjee[1] and Pradhan Anju[2]

[1]ICMR-NIMS, New Delhi
[2]ICMR, New Delhi

Background: Indian council of medical research (ICMR) conducted a quick one-day study to assess wastage of oral polio vaccine (OPV) being used in the pulse polio immunization (PPI) campaign in the country in 1999 covering 31,000 immunization booths located all over the country. The wastage of OPV was estimated to be 14.5 % with a wastage multiplier factor (WMF) of 1.17. Both these estimates were well below the assumed wastage and WMF as adopted in the program. Taking lead from this work, ICMR launched a much larger well designed multicenter study to assess percent wastage and WMF of six vaccines being used in the Universal Immunization Programme (UIP) of India. The study was carried out in 10 districts of four states of India.

Objectives: To determine the amount of wastage of vaccines being used under UIP; to determine the reasons of wastage of vaccine; to suggest methods for reducing the wastage of vaccine.

Methods: The study was conducted through the network of five human reproduction research centers (HRRCs) in ten districts located in four states of India. Wastage at the point of administration of vaccine was estimated.

Results & Conclusion: WMF and % wastage were calculated separately for each of the six vaccines for each district. The estimated % wastage and its range, the estimated WMF and its range for DPT, DT, TT, OPV, BCG and Measles was respectively 38.9% (12.8-69.7), 1.64 (1.15-3.31); 39.1% (27.3-61.4), 1.64 (1.38-2.59); 48.0%(20.9-67.1), 1.92 (1.26-3.04); 52.7% (22.1-75.7), 2.12 (1.28-4.12); 49.3% (30.3-70.2), 1.97 (1.43-3.36); 38.7% (20.8-50.1), 1.39 (1.26-2.00). The estimated % wastage of five of the six vaccines namely, DPT, DT, TT, OPV and Measles was found to be significantly higher than what is assumed in the UIP ($p<0.0001$). Among all the other reasons for wastage of vaccines, residual vaccine left in the vial was the most frequently reported reason for wastage of vaccines. Therefore, vials of variable size with house to house campaign were recommended to minimize wastage of vaccines in UIP.

mukherjeeajit@hotmail.com

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PERCEPTIONS OF CARETAKERS TOWARDS IPV VACCINE IN NEW DELHI, INDIA

Akanksha Rathi and Panna Lal
Dr. Baba Saheb Ambedkar Medical College and Hospital, India

Introduction: Over the last many years, a number of new childhood vaccines have been introduced into national immunization schedules. One of the most recently introduced vaccines in India is injectable polio virus (IPV) vaccine. One factor that determines the smooth conduction of any immunization program in the wake of introduction of a new vaccine is the knowledge and attitude of parents of the target infant population. No study has been done in North India to know the KAP of parents/caregivers of the children towards the newly introduced IPV vaccine.

Aim of Study: This study was conducted with an aim to know the gap in KAP of respondents towards introduction of IPV vaccine.

Methodology: This is a cross-sectional study done in a healthcare center of East Delhi in Mar'-Apr' 2016. A pre-tested and semi-structured questionnaire was administered (translated in native language) to all parents/respondents who came for the DPT-3 vaccine of their children.

Results: Out of the total 71 infants included in the study, 35 (49.3%) were males. The mean age of the children was 4.6±1.27 months. When asked about the knowledge of national immunization schedule, only 41(57.7%) respondents said that they are aware of the schedule. While majority (n=55, 77.4%) of the respondents knew that vaccination should be started at birth, only 12 (16.9%) respondents knew about the last immunization dose to be given at 16 years. Then they were asked about their attitude towards mild adverse reaction following immunization (AEFI) like fever and swelling of site of vaccination. Majority (n=56, 78.8%) of the respondents said that mild AEFI is not worrisome and is definitely not a deterrent to future vaccinations. When asked about the current immunization session, only 20 (28.1%) respondents knew that their child has been given 3 injections. 16 (22.5%) respondents revealed that the healthcare provider has not given them any information about the new vaccine.

Conclusion: The study reveals that though the attitude of parents towards immunization is majorly positive but the knowledge is lacking. The study also revealed that a substantial number of parents are not being made aware about the new vaccine being administered to their child that can have a negative impact on the immunization program.

akanksharathi.dr@gmail.com

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ENGINEERING ANTI-TUMOR IMMUNE RESPONSE WITH CUSTOMIZED FUNCTIONAL PROFILE

Arvind Chhabra
Amity University Gurgaon, India

Donor-specific anti-tumor T cells have been generated by engineering human primary T cells with tumor-associated antigen-specific T cell receptor (TCR) or chimeric antigen receptor (CAR). Both of these approaches have produced remarkable clinical outcomes, however, success rate of these approaches require significant improvement. In this context, availability of methods to generate T cells with customized effector function profiles would be useful. Although activation induced cell death (AICD) and program cell death (PCD) are essential immune homeostasis mechanisms, characterization of the mechanism of epitope-specific AICD in human primary T cells could help generate anti-tumor T cells that would sustain longer in the physiology and produce superior clinical outcomes. Utilizing human melanoma-associated antigen-specific anti-tumor T cell-derived MHC class I restricted transgenic TCRs, we have recently generated $CD4^+$ and $CD8^+$ multifunctional anti-tumor T cells. We have found that human melanoma-associated antigen-specific MHC class I restricted transgenic T cell receptor (TCR) engineered (TCR engg) $CD4^+$ and $CD8^+$ T cells exhibit differential susceptibility to epitope-specific AICD, such that while TCR engg $CD8^+$ T cells undergo AICD even upon encountering their target epitope for the very first time, TCR engg $CD4^+$ T cells become susceptible to AICD following one encounter with the target epitope. We have also characterized the mechanism of AICD in TCR engg human primary T cells and shown that JNK, BCL-family proteins, and p53-mediated non-transcription dependent pathway plays an essential roles in it. We will discuss different approaches being pursued towards generating long-lasting anti-tumor T cells with customized anti-tumor effector function profile that could help improve the efficacy of current immunotherapy approaches.

arvindac@yahoo.com

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SYSTEMIC AND PREDICTIVE TRENDS OF MULTIDRUG RESISTANT SALMONELLA TYPHI ISOLATED FROM WASTEWATER IN SUDAN

Ayman Elshayeb
Sudan

Background: Enteric fever has persistence of great impact in public health, it caused by *Salmonella enterica* that seldom detected in wastewaters of stabilization stations due to treatment processes

Objective: The aim of this study is to evaluate the recent state of antibiotics susceptibility of *Salmonella* Typhi with special concern to multidrug resistance strains and predict the emergence of new resistant patterns

Methods: *Salmonella* Typhi were isolated and identified according to WHO and ISO guidelines, the bacterial antibiotic susceptibilities were tested using the CLSI recommendations. The predictions of resistance emergence were done using logistic regression, forecasting linear equations and stochastic model.

Results: A total of 128 antibiotics resistant *Salmonella* Typhi strain were recovered from wastewater, they resisted antibiotics except ciprofloxacin. Current patterns of ciprofloxacin breakpoints interpretations were in susceptible ranges by disc diffusion (S≥20 mm), minimum inhibitory concentration was recorded as (I=16 µg/ml) and minimum bactericidal concentration= (R≥32 µg/ml). The probability of an isolate to develop resistance was plotted for MBCs the rate of resistance. The predictive patterns of resistance were spontaneously solved using exponential trend (y=ne) for each isolate at 16 µg/ml and 32 µg/ml of ciprofloxacin in certain period and the high values of coefficient R^2>0.5 indicate the rates of bacteria resistance incidence.

Conclusions: The current patterns of S. Typhi confirmed the increasing probability of emerging multidrug resistance according to frequent consuming, drug policy and bacterium genetic mutations.

ayman_elshayeb@yahoo.com

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ISSUES IN AFFORDABILITY AND ACCESS TO VACCINES AND THE ROLE OF THE VACCINE INDUSTRY

Balasubramaniam K V
Indian Immunologicals Ltd, India

Access to vaccines and their affordability are prime concerns in developing countries. While much has been done to address these critical determinants of immunization by multi-lateral agencies, there are many aspects related to the character and structure of the industry which are still to be effectively addressed. Chief among these are the non-egalitarian mission of vaccine companies, the oligopolistic character of the industry, lack of focus on vaccines for neglected diseases and pursuit of profit maximization. Compounding this at the field level are issues related to health system preparedness, delivery infrastructure, program errors, and to some extent the negative social and religious influence. It is imperative on the vaccine industry to shed its reticence and play a pro-active and egalitarian role to foster shared value with governments and the society, and thereby make immunization affordable and accessible to all.

kvbala2711@hotmail.com

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OUTCOMES AND FACTORS AFFECTING HIV STATUS DISCLOSURE TO REGULAR SEXUAL PARTNER AMONG WOMEN ATTENDING ANTIRETROVIRAL TREATMENT CLINIC

Bedilu Deribe
Hawassa University, Ethiopia

Introduction: HIV infected individuals face a number of challenges when they disclose their sero-status. Although discloser improves access to HIV prevention, increased opportunities for risk reduction and increased opportunities to plan for the future, HIV positive status discloser is lower in developing countries.

Objective: To assess outcomes and factors affecting HIV status discloser to regular sexual partner among women attending anti-retroviral treatment clinic at Hawassa University comprehensive specialized hospital.

Method: An institution based cross sectional study was conducted among 191 randomly selected HIV positive women attending Hawassa University referral hospital ART Clinic from Mar 1 –Mar 30 in 2017. The datawas collected after having ethical clearance letter from institutional review board and consent from client. Data were collected through interview using pre-tested questioners. The collected data was analyzed by using SPSS version 20. Bivariate and multivariate logistic regressions were done and final significantly associated factors were identified on the basis of OR with 95% CI.

Results: over all 72.9 of the women has disclosed their HIV status to sexual partners. Among those disclosed their HIV positive status, 54.1% get their freedom to have follow up. While 30% get their freedom to use condom. Negative outcomes associated with status disclosure were stigma 11.6%, discrimination 10.1% and psychological violence5%.Women who had rough relation with her 89% less likely to disclose their status as compared to women with smooth relationship (AOR=0.11 955CI 0.01, 0.119). Women who had children were 9.89 times more likely to disclose their status to sexual partners than their counter parts (AOR 9.89, 95% CI 2.68, 36.36).women who received counselling were almost 7 times more likely disclose their HIV status to their sexual partner (AOR=5.63 95%CI 2.24, 14.13) .

Conclusion: HIV positive status discloses to sexual partners was found to be low. HIV status disclosure was accompanied by both negative and positive consequences. Presence of offspring, counseling, relationship status before status disclosure was factors associated with HIV positive status disclosure.

bediluderibe2002@gmail.com

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DIRECT EVIDENCE OF VIRAL INFECTION AND MITOCHONDRIAL ALTERATIONS IN THE BRAIN OF FETUSES AT HIGH RISK FOR SCHIZOPHRENIA

Segundo Mesa Castillo
Psychiatric Hospital of Havana, Cuba

Introduction: There is increasing evidences that favor the prenatal beginning of schizophrenia. These evidences point toward intra-uterine environmental factors that act specifically during the second pregnancy trimester producing a direct damage of the brain of the fetus. The current available technology doesn't allow observing what is happening at cellular level since the human brain is not exposed to a direct analysis in that stage of the life in subjects at high risk of developing schizophrenia.

Methods: In 1977, we began a direct electron microscopic research of the brain of fetuses at high risk from schizophrenic mothers in order to finding differences at cellular level in relation to controls.

Results: In these studies we have observed within the nuclei of neurons the presence of complete and incomplete viral particles that reacted in positive form with antibodies to herpes simplex hominis type I [HSV1] virus, and mitochondria alterations.

Conclusion: The importance of these findings can have practical applications in the prevention of the illness keeping in mind its direct relation to the aetiology and physiopathology of schizophrenia. A study of the gametes or the amniotic fluid cells in women at risk of having a schizophrenic offspring is considered. Of being observed the same alterations that those observed previously in the cells of the brain of the studied foetuses, it would intend to these women in risk of having a schizophrenia descendant, previous information of the results, the voluntary medical interruption of the pregnancy or an early anti HSV1 viral treatment as preventive measure of the later development of the illness.

segundo@infomed.sld.cu

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VACCINES FOR MIGRANTS AND REGIONE VENETO PROTOCOL: AN UPDATE ON VACCINE COVERAGE IN THE APPLICANTS FOR INTERNATIONAL PROTECTION, IN THE HEALTH DISTRICTS 1 AND 2 OF THE AZIENDA ULSS 9, VERONA, ITALY

Daniele Spedicato[1], G Salandini[1], O Mariotto[1], P Cicco[1], E Finardi[1], N Pelacchi[1], A Brioni[2], L Colucci[2], C Postiglione[2] and O Bosco[2]

[1]University of Verona, Italy
[2]Service of Hygiene and Public Health of AULSS 9 Scaligera, Italy

Introduction: In the last few years, the World Health Organisation (WHO) and the European Centre for Disease Prevention and Control (ECDC) underlined the importance of assessing the vaccine coverage of the migrants, allowing them to have access to vaccinations in the countries of arrival. Since 2015, in the Regione Veneto, a protocol has been started up with the aim of monitoring infectious disease and immune prophylaxis in the applicants for international protection. The protocol offers free diphtheria-pertussis-polio vaccine (DP-IPV) and measles-mumps-rubella-varicella vaccine (MMRV).

Methods: Our service of public health carried out a cross-sectional, observational study analysing data from the computerized vaccine registry of the Regione Veneto, in order to quantify the subjects applying for international protection who had been given the DP-IPV vaccine and MMRV vaccine in 2017 in the health districts 1 and 2 of AULSS 9, as scheduled in the Regione Veneto Protocol.

Results: The analysis of the above-mentioned data showed that in 2017, our Service performed 584 new medical examinations on applicants for international protection (82.7% male, 27.3% female). 97.8% out of these 584 migrants are adults, and 9.2% comes from polio-endemic countries (Afghanistan and Pakistan). DP-IPV vaccine and MMRV vaccine were proposed to adults, while minors were suggested vaccines provided for in the national plan for vaccine prevention 2017-2019. Vaccine coverage in the adults turned out to be 100% of the examined migrants.

Conclusions: This protocol proved to be well accepted by the migrants and easy to manage, therefore helping to prevent new measles and varicella outbreaks in this vulnerable population (migrants applying for international protection), and at the same time contributing to maintain our country polio-free.

daniele.spedicato85@gmail.com

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COMPULSORY VACCINATION WORKS: UPDATE ON MEASLES AND POLIO VACCINE COVERAGE IN THE HEALTH DISTRICTS 1 AND 2 OF AULSS 9, VERONA, ITALY

Daniele Spedicato[1], G Salandini[1], O Mariotto[1], P Cicco[1], E Finardi[1], N Pelacchi[1], A Brioni[2] and Oliviero Bosco[2]

[1]University of Verona, IT
[2]Service of Hygiene and Public Health of AULSS 9 Scaligera of Verona, IT

Introduction: The n.119 national law dated Jul' 31st 2017 concerning urgent measures on vaccine prevention, infectious disease and controversies about drug administration was drawn with the aim of reaching and maintaining the vaccine coverage threshold up to 95% as recommended by WHO to guarantee herd immunity and furthermore assuring the adequate safety conditions related to highly contagious, potentially epidemic infectious disease.

Methods: Our service analysed data from the computerized vaccine registry of the Regione Veneto and compared the Jun 1st 2017 vaccine coverage with the one of Jun' 1st 2018, focusing on the third dose of polio vaccine and the first of measles vaccine of the 2014 birth cohort in the 1 and 2 health districts.

Results: Vaccine coverage for the third dose of polio vaccine and the first dose of measles vaccine increased significantly, according to data concerning the 2014 cohort: as a matter of fact, the vaccine coverage of the above-mentioned cohort were respectively 93,3% and 91,1% according to Jun' 1st 2017 data. The very same readings recorded on June 1st 2018 showed a 2.1% increase for the third dose of polio vaccine, reaching 95.4% coverage, and a 4.1% increase for the first dose of measles vaccine, raising the coverage percentage up to 95.2%.

Conclusions: At almost a year after the national law regarding the compulsory vaccination for educational services came into force, a positive trend in the vaccine coverage has been recorded after 24 and 36 months. In particular, in the health districts 1 and 2 of AULSS 9, the vaccine coverage for the third dose of polio vaccine and for the first dose of measles vaccine has reached the 95%. Besides, 24.2% of the people who had not completed the polio vaccination course are in any case undergoing the vaccine iter required by the obligation, since they have already been given the second dose of polio vaccine.

daniele.spedicato85@gmail.com

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EFFECTIVENESS OF THE RESPONSE TO THE EBOLA EPIDEMIC IN GUINEA 2014-2016 (LESSONS EARNED AND RECOMMENDATIONS MADE)

Alpha Mahmoud Barry[1], Sakoba Keita[2], Robert Camara[3], Pepe Pilivogui[4], Batchilly[5] and Mandjou Diakite[6]

University Conakry, Guinea

During the 2014 Ebola outbreak in Guinea, the Ministry of health with the support of international partners, set up a National Strategy to stop the disease propagation and control the epidemic all over the country. A year later, a qualitative survey within the most affected areas including the health district of Gueckedou, Forécariah, Coyah, and Conakry in which around 100 people were questioned. The in depth interviews targeted stakeholders, partner organization managers, center of Ebola care and treatment managers, community leaders, traditional hailers , mass media officers, community animators, and secured burial teams and the focus group discussion with youths, women association, health workers, community members. The mains objectives of the evaluation were to pinpoint the overall effectiveness of the epidemic control activities; know the perceptions and the lessons learned during the epidemic; gather the main recommendations to the control of epidemic like Ebola in a given country. The evaluation results showed that: The majority (90%) of the interviewees has never heard about Ebola before the outbreak of 2014, those who have heard were informed during their training in medical school (virology) or via mass media on the previous epidemic in RD Congo. (85%) of them declared being reached through infection of a family member, neighbored, colleague or a well-known health professional. Seven out of 10 interviewees recognized the plus values and the efficiency of the international organization supports help to control of the epidemic think the disease was sent by stringers for experimentation purpose. The most contributing activities to the outbreak control were the multimedia communication (70%), the case management (70%), and the distribution of hygiene kits (90%) (hand washing devices, soap, and chlorine), and the national committee coordination (40%), the training of the response actors, the community engagement (90%), and the strengthening of the laboratory system (50%). The weaknesses of the Ebola response were: the discrepancy of the early message spread (which caused fear and panic among the population); the late of funding and international intervention; the multiplicity of the managing protocol used by the various partners; the "low level of skill of health workers to the prevention and infection control; the late of the community engagement and the reticence occurred. The majority of interviewees recommend that most important action to be taken to control an epidemic, like Ebola, should be: an early deflation of the epidemic by WHO; a quick and efficient international mobilization; an efficient carefulness actions to save the victims; an harmonized information about the epidemic; an early involvement of all actors including Communities leaders, Socio-anthropologists, traditional healers, youth women association; Almost all interviewed agreed on that the harm and the socioeconomic impact of Ebola in Guinea were related to the weaknesses of the country health system and the neglected of the early community engagement to the control activities.

alphaguinea@gmail.com

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CAPACITY BUILDING THROUGH TRAINING OF 120 LABORATORY PROFESSIONALS IN BIO RISK (BIOSECURITY AND BIOSAFETY) AND BIO THREAT RISK REDUCTION IN GUINEA CONAKRY, 2016-2017

Alpha Mahmoud Barry[1], Natasha Griffith[2], Fares Khalid[3], Lamine Koivogui[4], Aboubacar Savané[5]

[1]University of Gamma l Conakry- DG Sante plus
[2]UCLA/CDC Atlanta /CRDF GLOBAL
[3]University of Fez Morocco
[4]National Institute of Public health/ Referral National Laboratory
[5]Bio medical National Laboratory Network

The world's most widespread epidemic of Ebola Virus Disease (EVD) began around December 2013. Within six months, cases were found throughout Guinea, Liberia and Sierra Leone, countries that eventually suffered 28,616 cases and 11,310 deaths due to the outbreak. Initial response was marked by disease surveillance gaps and weaknesses but heroic efforts eventually led to monumental successes. Laboratory infrastructure in these countries was weak and unprepared to respond effectively. In Guinea, Santé plus Organization, the Ministry of health /National Laboratory Direction, with the support of CRDF GLOBAL and EMPHNET organized seven (7) training of 120 peripheral laboratory agents in Bio risk (biosecurity and biosafety). The mains objective was to contribute to Guinea laboratories' system straightening on bio threat and bio risk reduction thought increase capacity building of laboratory agents in biosecurity and biosafety. At the end, 120 participants have accomplished (certification) their training with an average of participants' knowledge increased up to 80%. During the training sessions, some lessons were learnt including: the Full implication of administrative and health authorities the great interest and satisfaction of participants to the topics covered. After 12 months following the regional training sessions on bio risk training sessions, a Qualitative survey involving 110 out of 120 professional who completed the training sessions organized: 110 /120 are in place working in their laboratory among with 90% declare sing their skills after training to improve their biosecurity procedure especially the west management and the biomedical sample management (collect, conditioning and transfer); More than half (60/110) interviewee declare "training their colleague on the use of the EPE"; Almost all of interviewee (90100/110) declare "having organized sensitization sessions either with stakeholder or with the Community to address the bio threat risk prevention especially in with Ebola Forecaria and Gueckedou place where Ebola have killed the most. Many of interviewee (80/110) declare "improving the west management quality in their lab"; (40/110) interviewee declare "the need of a National bio risk policy in Guinea". Many of the trainees (100/110) would like to be part of the Guinea bio risk organization to promote the biosecurity, biosafety and the bio threat risk reduction in Guinea.

alphaguinea@gmail.com

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IMMUNODOMINANCE, DECEPTIVE IMPRINTING AND IMMUNE REFOCUSING TECHNOLOGY: BLUE PRINT FOR DERIVING NEXT GENERATION BIOLOGICALS FOR DIFFICULT MICROBES

Peter Lloyd Nara
Biological Mimetics Inc., USA

Over the last 250 years, the use of vaccines, a mainstay of preventative medicine and public health mainly in the infectious diseases area has proven to be one of the most successful and cost-effective medical interventions ever discovered. Despite these great advances to human and animal health of the past 5 decades; the basic immunologic principals and technology does not work for the most part against the many remaining pathogens and many cancers of humans and animals. This is mainly due to a combination of evolved host evading strategies of both infectious pathogens and cancer cells and the yet unappreciated aleatory characteristics inherent within the vertebrate immune system. These combined make them inherently more capable of outsmarting the host defense systems. Phenomena such as strain- and serotype-restricted immunity, antigenic variation/mutation, poor anamnestic memory, disease-enhancement and incomplete immunity, all are major gaps in our understanding of the complex host evasion mechanisms that have evolved. Deceptive imprinting is at the heart of a new understanding of how the hosts response to mutable infectious pathogens and cancer cells to create a molecular diversion (decoy) at the level of both the innate and acquired immune host defense systems, much like how metallic chaff would confuse a radar system trying to locate a missile or plane. On an immunologic level, immunodominance, repertoire sculpting and antigenic variation are coupled such that host immune responses are directed to more immunodominant and non-protective structures resulting non-protective B and T cell immune responses. To circumvent this host evading mechanism, we have developed a first generation technology called immune refocusing that has been designed specifically to reorder the non-protective immunodominance by identifying/mapping the decoy epitopes and molecularly removing or attenuating it thus redirecting the host immune system to the more protective regions of the microbe. This lecture will bring together those aspects learned from studying infectious diseases pathogens in new paradigm shifting first principals of deceptive imprinting and immunology and those of cancer biology in hopes of developing new insights from querying pathogen genomes through pressure point technology and application of the technology of immune refocusing. These paradigm shifting scientific insights have opened up fresh new approaches to technical advancement and the development of new antigens that can be used for vaccines and deriving new monoclonal antibodies toward inducing improved and broader protective immunity for both infectious diseases and cancer.

nara@bmi-md.com

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SUCCESSFULLY ACTIVATING POSITIVE BEHAVIORS OF THE STAKEHOLDERS INVOLVED IN VACCINE PURCHASING AND USAGE THROUGH TECHNOLOGICAL ADVANCES

Pierre A Morgon[1, 2]
[1]MRGN Advisors, Switzerland
[2]Virometix A, Switzerland

The vaccine segment is anticipated to be one of the fastest growing one of the healthcare industry and several leading firms have stepped up vaccine investments in recent years. Unlike therapeutic agents, vaccines are administered to healthy individuals only once or very infrequently during a life time. Vaccines generate well-documented positive externalities, yet their poor awareness and acceptability among vaccine end-users may contribute to resurgence of transmissible diseases and consequently trigger governmental interventions such as mandating vaccination. In addition to technical and clinical development per the highest quality standards, bringing new vaccines to market requires carefully orchestrated programs targeting the multiple types of stakeholders along the entire value chain and addressing their respective purchasing behavioural drivers. Against a backdrop of anti-vaccination buzz and vaccine fatigue, successful global launch and sustainable usage of a vaccine requires the development of a multi-pronged strategy addressing all aspects in relation to acceptability (e.g. the motivation to immunize despite the quasi-disappearance of the disease), accessibility (e.g. supply chain services), availability (e.g. mechanisms ensuring reliability of supply) and affordability (e.g. tiered pricing policy taking country differences in per capita income into account). Leveraging novel technological advances can positively influence the ability to activate these levers successfully.

pm@mrgnadvisors.com

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STUDY OF FACTORS LIMITING UNIVERSAL ACCESS AND USE IMMUNIZATION SERVICES IN THE AFRICAN CONTEXT

Alpha Ahmadou Diallo[1], Peter G[2], F Biro Diallo[3] and Mahi Barry[4]

[1,2,3,4]University Conakry, Guinea

The review of the factors hindering access to vaccination and the process of accompanying the actors as part of the plan for strengthening social mobilization and communication capacities to remove barriers to access to vaccination for all. The main measures taken are: 1) the commitment of the program and district management teams to assume their functions; 2) Upgrading vaccinating agents to acquire the necessary knowledge, skills and attitudes that encourage the vaccination of targets by trust; 3) the promotion of good practices towards change, reason for the program through the opportunities to communicate differently and to share data in favor of vaccination: Involvement of the press, distribution of SMS by telephone operators, alliance with Religious, promotion of vaccination in schools so that students are vectors of good information on vaccination in their family, social networks, publication of a bulletin on vaccination, involvement of artists and promoters of culture, incentives/ promotion, action research development, on-going systemic data analysis, advisory support, integrated supervision, program review, local funding for immunization.

dalphahm@yahoo.fr

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HUMAN HERPESVIRUSES: SHOULD WE STILL INVEST IN VACCINES OR FOCUS ON PREDICTIVE TESTS?

Emmanuel Drouet
Université Grenoble-Alpes, France

Human herpesviruses (HHV1-8) have co-evolved through a persistent infection in the host, spread efficiently to others generally without causing serious disease. The complex interplay between host and virus has made it difficult to elaborate useful vaccine strategies to protect against the HHV-associated diseases. The Varicella-Zoster vaccine represents the paradigm of a successfully marketed herpesvirus vaccine. Over the years, the development of HHV vaccines has been a story of mixed fortunes, especially for HSV-2 and HCMV. However, studies carried out in various disease settings (i.e. transplant patients or pregnant women), have emphasized the importance of cellular immunity and it is indeed encouraging to see that recent HHV vaccine (i.e. HCMV) development programs have started to incorporate this arm of the immune system. Nowadays, an array of arguments calls for a realistic goal for vaccine strategies which should be preventing HHV disease rather than HHV infection. It is particularly, the case for the Epstein-Barr virus (EBV or HHV4) which is the primary cause of infectious mononucleosis and is associated with epithelial cell carcinomas, as well as lymphoid malignancies. The challenge is that the HHVs express very different proteins during their lytic and latent phases. Parallel to this need, one could propose priorities for future research: identification of surrogate markers that predict the development of HHV diseases or malignancies; determination of immune correlates of protection against HHV infection and disease in animal models and in humans. Finally, we will discuss recent works showing the beneficial role of these persisting viruses in the context of malignancies.

Emmanuel.drouet@ibs.fr

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SEROLOGICAL INVESTIGATION OF RACEHORSE VACCINATION AGAINST EQUINE INFLUENZA IN MOROCCO

O Fassi-Fihri[1], M Dilai[1], M Piro[1], S Fougerolle[2, 3], M El harrak[4], W Maher[5], R El mourid[5], L Legrand[2, 3] and R Paillot[2, 3]

[1]Hassan II Institute for Agronomy and Veterinary Medicine-Rabat, Morocco
[2]Universite de UniCaen Normandie-BIOTARGEN, France
[3]LABÉO Frank Duncombe, France
[4]MCI Animal Health, Morocco

In order to evaluate the vaccination status and the protection level against equine influenza (EI) virus infection in racehorses, a serological investigation was carried out on 509 racehorses from 6 different regions in Morocco using three serological tests: enzyme-linked immunosorbent assay (ELISA), hemagglutination inhibition (HI) and single radial hemolysis (SRH). The serological analysis showed 56% of seropositivity (285/509) by ELISA, 67% (343/509) by HI and 89.4% (455/509) by SRH, with 69.9% (356/509) above the clinical protection threshold, 19.4% (99/509) with low non-protective antibodies SRH titers and 10.6% (54/509) of horses with no SRH antibodies. Using the Kappa test, the SRH and HI assays showed a strong agreement, the SRH and ELISA assays had a moderate agreement and the HI and ELISA assays showed a poor agreement, which confirmed the low sensitivity of the ELISA assay when compared with the other serological methods. Seropositivity was positively correlated with the age of horses and the number of EI immunization received. The EI vaccines used had a weak influence on the serological status. This effect was observed when the EI vaccines Calvenza® (Boehringer Ingelheim) and Fluvac Innovator® (Pfizer) were used, with 94.1% and 100% of seropositivity when measured by HI, and with 100% and 94.7% exceeding the clinical protection threshold using (SRH), for these two vaccines respectively. The EI vaccine Fluvac Innovator® was administered prior to importation into Morocco (this vaccine was not commercialized at the time of the study). Other EI vaccines, including Prequenza-Te® (MSD Animal Health) (the most frequently used in Morocco with 67% coverage (342 horses out of 509 studied)) and Proteqflu-Te® (Boehringer Ingelheim) (22% coverage (114/509)) did not influence the serological status; with 64% and 67.5% seropositivity (HI) and with 66.4% and 72.8% above the clinical threshold (SRH), respectively. The location and the time since last vaccination have no influence on the serological result. Several factors relating to humans, vaccination or horses could influence this serological status.

o.fassifihri@iav.ac.ma

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ANALYSIS OF ANTIGEN CONSERVATION AND INACTIVATION OF GAMMA-IRRADIATED AVIAN INFLUENZA VIRUS SUBTYPE H9N2

Iraj Khalili[1], Farahnaz Motamedi Sedeh[2] and Bahareh Salehi[3]

[1]Razi Vaccine and Serum Research Institute, Iran
[2]Nuclear Science and Technology Research Institute, Iran
[3]University of Tehran, Iran

Avian influenza A subtype H9N2 virus belongs to *Orthomyxoviridae* family and causes low pathogenic disease avian influenza. The use of gamma irradiated viral antigens has been developed in the production of effective vaccines. In this research LPAIV H9N2 strain, A/Chicken/IRN/Gazvin/2001 was multiplied on specific pathogen free (SPF) eggs and irradiated by a Nordian gamma cell instrument. Irradiated and non-irradiated avian influenza virus (AIV) samples were titrated by EID50 method and hem¬agglutinin antigen were analysed by Hem¬agglutinin test as the WHO method. Infectivity of irradiated virus was determined by eggs inoculation method during four blind cultures. The results showed after increasing dose of gamma radiation, virus titer decreased gradually. D10 value and optimum dose for complete virus inactivation were calculated by dose/response curve, 3.36 and 29.52 kGy, respectively. Also, HA antigenicity of gamma irradiated virus samples from 0-30 kGy was not changed. The results of safety test for gamma irradiated AIV samples showed complete inactivation with gamma ray doses: 30 and 35 kGy without any multiplication on eggs after four blind cultures. According to the results of HA antigen assay and safety test, the gamma irradiated and complete inactivated AIV subtype H9N2 is a good candidate as an inactivated immunogenic agent for poultry vaccination.

Iraj_dv4953@yahoo.com
I.khalili@rvsri.ac.ir

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MENINGOCOCCAL VACCINES

Javier Casellas
Vaccine Expert Consultant, Argentina

Neisseria meningitidis causes severe, often fatal septicemia and meningitis. New polysaccharide-conjugate vaccines against four serogroups (ACWY) are now in use in many countries due to increase in W disease and epidemiological unpredictability. Since serogroup B contributes significantly to the burden of meningococcal disease in many industrialized and developing countries where both epidemic and endemic serogroup B infections occur, new vaccines are available against this serogroup as well. Vaccines effective against specific strains responsible for serogroup B disease have been licensed and have been included in National Immunization Programs with great success. The epidemiology and pathogenesis of meningococcal disease are detailed, along with discussion of the new advances on vaccine prevention of ABCWY meningococcal disease.

javier_casellas@outlook.es

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VIRUS LIKE PARTICLES AS A SCAFFOLD FOR MENINGOCOCCAL VACCINE DEVELOPMENT

Murtala Jibril, Emil Carlsson, Sebastian Aston-Deaville, Jeremy Derrick

University of Manchester, UK

Neisseria meningitidis **is a Gram-negative bacterium and causative agent of life-threatening meningococcal disease in humans (meningitis and septicaemia). The conventional approach of capsular polysaccharide (CPS) usage as a platform for meningococcal vaccines' development has been very effective with serogroups A, C, W135 and Y, but limited effect with serogroup B (MenB) due to antigenic similarity of its CPS with human antigen. A well-studied virus-like particle (VLP), Hepatitis B core antigen (HBcAg) was used as a scaffold to incorporate meningococcal surface antigens. The VLP-antigen fusion proteins were expressed, purified and characterized by SDS-PAGE analysis, circular dichroism and transmission electron microscopy. Uptake of the VLP-antigen fusion proteins by THP-1-derived dendritic cells and macrophages was carried out *in vitro*. Intracellular co-localization and upregulation of surface markers were assessed by cell culture, ImageStream and FACS analysis. The VLP-antigen proteins were shown to be taken up by clathrin-mediated endocytosis and macropinocytosis and co-localized in lysosomes. They also significantly stimulate higher upregulation of HLA-DR, CD80, CD206 and CD209 on macrophages compared to the antigen alone.**

murtala.jibril@manchester.ac.uk

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RESPONSIVENESS OF VACCINES TO HUMANS IN KENYA: EXAMINING SAFETY AND EFFICACY OF HUMAN VACCINES

Johnstone Mutua
Kisii University, Kenya

Vaccination is not only recognized as the most cost-effective form of health care but also it's the most efficient and effective way of preventing infections. Despite recent report showing big support for vaccination in communities, few issues need to be addressed i.e. the safety of vaccines to human health, adverse effects and transparency in public involvement in vaccination programs in the country. Studies made to investigate the acceptability of vaccines and identify the determinants to low and high levels of acceptability noted; doubts on safety of vaccines, occurrences of deaths due to vaccination and lack of awareness of adverse effects of vaccines as barriers to achieving high vaccination rate in Kenya. For example, from recent polio vaccination program, symptoms like skin rashes, convulsion, fever and diarrhea were reported. For transparency sake, safety and assurance; the government should explain as to why shift from trivalent polio vaccine which had fewer adverse symptoms to upgraded bivalent vaccine which gave much worries to most parents. Yes, it could be very true these adverse effects are as a result of influenza outbreak in most part of the country as the ministry of health stated but claims that the vaccines may have been contaminated should thoroughly be investigated and epidemiological investigation should be carried out in cases of outbreak of other infections that could worsen effects of vaccines. Earlier this year in Bomet County, a child died and four other admitted in hospital as a result of measles vaccines. At the same time, children aged 9 and 12 months responded to the vaccine by swelling. Other places within the nation had report of the deaths of several children. The government stated that death in some children was as a result of ignorance by mothers from dangers of repeated dosage and Vitamin A supplement within a short span. Others were thought to have died of other ailment apart from effects of vaccination. Health personnel should critically take the issue of repeated dosage to prevent more deaths on the same. In Kenya, it was reported that the Church ill advised its members on tetanus vaccination despite it been involved in all meetings to discuss the jabs. The church claimed that the vaccine is not safe to be used on Kenyan citizens as it had fertility issues among women. A study published in American journal of tropical medicine and hygiene gave differences in tetanus vaccination rate between men and women in Kenya. This was due to deaths of men as a result of vaccination with tetanus vaccine. Based on the above claims, the question remains how safe and efficient is human vaccines on population. If an outbreak of other diseases could mean mortality upon vaccination, then more research should be done to counter the lethal effects that could arise. With deaths on children and adverse effects upon immunization, thorough studies should be carried out to reduce deaths that have occurred and assure the public of safety of their children. Disparities that arise as to why only women are vaccinated and men are not should be addressed as to why the tetanus vaccine caused deaths in men with East Africa countries. A lot research has to be done and measure has to be put into place on vaccines to ensure health on our future generations.

jiohntua@gmail.com

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MEASLES ELIMINATION IN DEVELOPING COUNTRIES: HIGH TIME TO CHANGE THE STRATEGY

Joseph L Mathew
APC-PGIMER, India

Measles remains one of the world's largest public health problems especially in developing countries. Current guidelines in these countries recommend vaccination at 9 months of age expecting infant protection through maternal (transplacental) antibodies till then. More recently, second and third doses of measles containing vaccine have been introduced at 12-15 months and 4-6 years. However, clinical experience confirms occurring of measles even before 9 months of age. Prospective cohort studies were conducted by my research group in 2005 and 2015 (coinciding with 20 and 30 years of universal vaccination in India) to evaluate measles susceptibility in infants and to identify the appropriate age for vaccination. In these studies, anti-measles IgG antibodies were measured by quantitative ELISA in 60 and 130 infants at birth, 3 months, 6 months, and 9 months (prior to vaccination). Susceptibility was determined by antibody titre <200 mIU/ml. The first study (2005) showed that 0%, 12%, 51% and 100% infants were susceptible at birth, 3 months, 6 months and 9 months respectively. The second study (2015) confirmed susceptibility in 0%, 23%, 84%, and 100% infants. Preterm infants were more susceptible that term infants at 3 months and 6 months. More recently in 2018, we have concluded a larger study with over 200 infants and observed similar findings. Emerging data from China also suggest a similar situation. These data suggest that most Indian and Chinese infants become susceptible to measles well before the age of vaccination. Further the two time series showed that more infants were susceptible in recent years than 2005; this could be due to greater proportion of mothers having vaccine-induced immunity than natural immunity. These data argue for earlier (rather than later) vaccination with measles vaccine in India, China and probably other developing countries also. This necessitates an urgent, evidence-based change in the guidelines and the overall strategy.

dr.joseph.l.mathew@gmail.com

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VETERINARY VACCINES: PRESENT SITUATION AND DEVELOPMENT POSSIBILITIES

Szilard Kraxner
Kraxner Kft, Hungary

This presentation wants to show the differences between companion animal vaccine and swine vaccines regarding the clients, epidemic situation and possible developmental directions. Small animal practioners have got a guideline for the vaccination of dogs and cats (WSAVA vaccination guidelines group). There are core vaccines and possible administered vaccines. In Hungary, the epidemic situation is quite good; diseases related to core vaccines are very rare and well controlled. Clients of companion animal practioners have got the same attitude than clients of general practioners. Recent development of vaccines was completion of vaccines with new Leptopsira strains (4 instead of 2), new route of application Para influenza vaccine (kennel coughing). There were weak efforts to control babesiosis, the vaccine was withdrawn from the market. Developmental possibilities are from business point of view less promising as in swine practice. Swine practioners are in completely other situation: changing of a vaccination system needs a decision process. Farm manager/owner as client is strongly involved. We should regard this changing as it would be a change of technology in a factory. The livestock industry still is using lot of antibiotic that should be reduced. Vaccines are good opportunities to reduce administered antibiotics, but there are several diseases where we have not got any vaccines or the effectiveness should be improved. Para typhus, ileitis, dysentria need several times antibiotic treatment and the vaccination solution is not resolved. Regarding ileitis, it is one of diseases where antibiotic treatment was far cheaper as vaccination. There was several good developments in last years: At administering of vaccine, the transmission of infection was blocked with an intradermal automatic device. The result was not only a safer way but a better effectiveness of vaccination. Several efforts were made to construct polivalent vaccines which can save lot of physical work and stress for piglets. My opinion is the farm should consider his own situation before choosing polivalent vaccines.

vetkraxner@invitel.hu

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HUMAN VACCINATION: CURRENT TRENDS AND CHALLENGES IN HUNGARY

Gergely Krizsan
Locum Consultant Microbiologist, Hungary

Vaccine-preventable infectious diseases continue to represent a significant challenge in Europe due to various reasons. These include the spreading reluctance of parents to get their children vaccinated, the quality and efficacy of vaccines, concerns of revaccination to provide long-term immunity, vaccination of pregnant women, financial issues, geographical mobility and recent outbreaks in Europe, particularly measles. The vaccination rate in Hungary is traditionally very high, almost 100% due to the good compliance. The vaccination schedule is also updated on an annual basis according to current trends and requirements. These changes include the introduction of obligatory pneumococcal conjugate vaccine (PCV-13) from 2 months (in 2014) and offering human papilloma virus (HPV) vaccine for girls at the age of 12 years (bi-, tetra- and nonavalent vaccines are available). Current issues relate to meningococcal vaccines that are available but not financially supported. Vaccines against B and C serogroups of *Neisseria meningitidis* are recommended to certain groups of people, being the two most prevalent serogroups in Hungary in the last few years with a strong dominance of group B (32 out of 48 cases in 2016/2017 season). There are similar concerns about rotavirus and chicken pox vaccines which may be the next new obligatory vaccine in Hungary. Other experts suggest serological screening for varicella to check immunity. The most important non-obligatory vaccines in Hungary may be considered: the meningococcal vaccines: group C or groups A,C,Y,W-135 and group B because of the high lethality of systemic meningococcal infections; HPV vaccines because of the oncogenicity of certain serotypes; hepatitis A vaccine due to recently increased incidence in Hungary and neighbouring countries; vaccine against tick-borne encephalitis (FSME), as the number of reported cases has been increasing in several European countries including Poland and the Czech Republic.

gergely.krizsan@gmail.com

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BROADLY NEUTRALIZING ANTIBODY KNOCK-IN MODELS AS LEAD DISCOVERY PLATFORMS FOR IDENTIFYING NEW HIV VACCINE APPROACHES

Laurent K Verkoczy
Duke University, USA

A truly effective HIV vaccine will likely require rapid and robust elicitation of broadly neutralizing antibodies (bNAbs), but the pathways to achieve this remain elusive. A critical roadblock has been the lack of practical animal models for reliably tracking development of bNAb responses to HIV vaccination. This talk will overview the various humanized immunoglobulin mouse strains we and others have collectively developed and/or are using for HIV vaccine research over the last decade, in order to highlight how they are helping to rank candidate regions in the HIV-1 envelope (Env), for which it may be most feasible for vaccination to induce bnAbs against. First, the pre- and post-immunization repertoires of various bNAb knock-in (KI) models we have engineered to produce unmutated precursor B-cells of various prototype bNAbs will be presented, to illustrate how such models can be effective tools in pinpointing mechanisms limiting bNAb development. Then, bNAb responses elicited in two of our recent knock-in models will be described, which are specifically directed to the V2 apex (a region in Env to which bNAb responses in infected donors arise more rapidly and frequently, and require less somatic mutation to develop), to further support the notion that the V2 apex may be a relatively more tractable HIV vaccine target. Our KI's V2 apex-specific responses will also be presented to demonstrate how such models can serve as practical lead testing platforms to iteratively down-select HIV immunogens or vaccine regimens re-designed to more selectively trigger bNAb responses and/or overcome any remaining impediments to their induction.

lverkoczy@SDBRI.org
laurent.verkoczy@duke.edu

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COLEY'S TOXINS AND THE CURRENT HYPE ON CANCER VACCINES

Matthias Giese
Institute for Molecular Vaccines Heidelberg, Germany

Already in the 1890s, William B Coley injected streptococcal organisms in patients with solid tumours (Coley's toxins) to activate the immune system. Coley (1862-1936) was an American bone surgeon, cancer researcher and pioneer of cancer immunotherapy. He was convinced that post-surgical infections had helped patients to recover better from their cancer by provoking an immune response. Because of severe adverse effects due to the living streptococcal organisms, he switched to use dead bacteria. But Coley's published results were difficult to interpret with confidence. More research would be needed to determine what benefit, if any, this therapy might have for people with cancer (American cancer society). Nevertheless, William B Coley is known as the Father of Immunotherapy.

Modern cancer vaccines : Prophylactic cancer vaccines may be an option in case of involvement of viruses such as human papillomavirus (HPV) and cervix carcinoma or other microorganisms. This anti-HPV vaccine is in a classical sense an antiviral vaccine only and can prevent a chronic inflammation. Chronic inflammation causes genotoxic stress in form of mutations or genomic instability and is known to enhance angiogenesis and tissue remodelling. Chronic inflammation has a deep impact on tumour initiation. It takes about 20 years from HPV infection to cervical cancer. The typical time course of the infection begins with HPV acquisition in adolescence and early adulthood, around 17-25 years, and cancer arises around 45-60 years. During this dark period accompanied with chronic inflammation innumerable mutations took place finally resulting in cancer. So far, there are no clinical data demonstrating anti-tumour efficacy of the diverse commercialized anti-HPV vaccines. Prophylactic cancer vaccines may be no option for cancer diseases caused by other agents beside microorganisms. The high mutation rate in tumour cells can generate a mutational load of 1-10 mutations per mega base of coding DNA. The prophylactic selection of proper tumour antigens would be a lottery, an endless cycle of try and error. The genetic instability produces permanent changes of epitopes. The efficacy of therapeutic cancer vaccines is still disappointing. Since the first scientific report on an experimental autologous (personalized) cancer vaccine (whole tumor homogenate, mixed with Freund's adjuvant and 3X injected intramuscularly in patient) was published 1964, the clinical efficacy of cancer vaccines was not as expected until today. Clinical validation remains elusive. The reduced efficacy of vaccines in the elderly is generally attributed to immunosenescence. Age-associated immune changes take place in the innate and acquired immune systems and affect not only lymphocytes, but also myeloid cells with a change in pro-inflammatory cytokines. The functional decline that characterizes aging begins after sexual maturity. Thymus involution begins with the puberty by the early teens.

Conclusion: Immunotherapy by vaccination is possible but a question of timing. Immunosenescence, immune dysfunctions are not limited only to the normal process of aging but also linked to cancer diseases. It makes no sense at all to vaccinate a cancer patient suffering from loss of important immune functions. A risk analysis of several parameters before vaccination could help to understand the current disposition of the immune system: makes a therapeutical vaccination sense or not.

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KNOWLEDGE, ATTITUDE AND PREVENTIVE PRACTICES TOWARDS SEXUALLY TRANSMITTED INFECTION AMONG PREPARATORY SCHOOL STUDENTS OF ARSI NEGELLE TOWN

Nega Degefa Megersa
Arbaminch University, Ethiopia

Background: Sexually transmitted infections (STIs) are a major global cause of acute illness, infertility, long-term disability and death with serious medical and psychological consequences of millions of men, women and infants. Due to their high prevalence, particularly in developing settings, STIs result in substantial productivity losses for individuals and communities, particularly where the majority of the population is less than 40 years of age.

Objective: to assess knowledge, attitude and preventive practices of Arsi Negelle preparatory students towards STIs.

Methodology: institutional based cross-sectional study design and quantitative method of data collection were employed. A Proportionate Stratified random sampling technique was used and finally, a total of 303 respondents were selected by systematic random sampling method. A standardized self-administered questionnaire was used to collect information from respondents

Result: half of the respondents (50.8%) had good knowledge about STIs and 54.5% of respondents were identified to have positive attitude towards STIs and 38.6% of respondents had good preventive practice despite the fact that the rest 61.4% had poor preventive practice towards STIs.

Conclusion: most of respondents had heard about STIs in one or another way however nearly half of respondent's have good knowledge regarding STIs. This study had called for continued and strengthened health education.

negshd05@gmail.com

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HUMORAL IMMUNE RESPONSES TO COMMERCIALLY AVAILABLE EQUINE INFLUENZA VACCINES IN AGED HORSES

Lean M S[1], Reedy S E[2], Chambers T M[2], Betancourt A[2], Horohov D W[2] and Adams A A[2]

[1]Aberystwyth University-IBERS, UK
[2]GLUCK Equine Research Centre, University of Kentucky, USA

Age-related decline in immune responses of geriatric horses is associated with a reduced response to vaccination and increased susceptibility to equine influenza virus (EIV) infection. The aim of the present study was to compare and evaluate the immune responses of geriatric horses given 2 doses of 'live' or 'killed' EIV vaccines. 27 geriatric horses (>20 yrs) were used in this study, all of which had prior exposure to equine influenza (EI) vaccination or infection. Treatment groups were stratified based on HI titres and body condition scores: Group 1 (n=7) 'killed' Calvenza™ EIV vaccine (OH/03 and KY/95, and Newmarket/93), Group 2 (n=7) inactivated Fluvac Innovator® EIV vaccine (KY/97) and Group 3 (n=7) 'live' canarypox vectored Recombitek® EIV vaccine (KY/94 and Newmarket/93). Group 4 (n=6) served as the non-vaccinate controls. Serum samples were collected prior to vaccination (day 0) and on days 7 and 14 post vaccination. 14 days (day 28) after the first vaccination, a second vaccination was administered, and serum samples were collected on days 35 and 42. Antibody responses were measured by HI, SRH and ELISA. Results showed that no significant difference (P>0.05) in HI, SRH and ELISA antibody titres for the control horses throughout the study. Post vaccination, there was a significant (P<0.05) increase in HI, SRH and ELISA antibody titres for all three vaccine groups between day 0 and day 7. No significant difference (P<0.05) was seen for groups between day 7 and 14, or between day 14 and 21, or between day 21 and 28 (2nd vaccination). Both 'killed' vaccines induced a significantly (P<0.05) higher antibody response measured via HI, SRH and ELISA when compared to the 'live' canarypox vectored vaccine. Our results show that whilst aged horses possess baseline antibody titres to EIV antigen through previous infection and or vaccination, vaccination with either killed or live vaccines can boost this response.

melslean@hotmail.com

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SAFETY OF VACCINES FOR PREGNANT WOMEN AND ROLE OF REGULATORY SYSTEM RELATED THE ISSUE

Merita Kucuku

National Agency for Medicines and Medical Devices, Romania

A vaccine is the most cost-effective measure available to protect and promote public health and this principle applies to use for vaccination of pregnant women. Pregnant women and newborn infants are at increased risk of complications from certain vaccine-preventable diseases (e.g., influenza, pertussis). The pregnant women in the US are 4-fold greater risk for hospitalization because of A/H1N1 infection than the general population. Maternal vaccination is an effective approach to prevent certain infectious diseases because it directly protects the mother and indirectly protects her newborn through passive antibody transfer. Clinical investigation and definitions for the assessment of outcomes should help expedite a variety of aspects of vaccine development as well as regulatory decision making. The reduction of child mortality by two- thirds in between 1990-2015 is the millennium development goals. The vaccines Tdap and inactivated influenza are routinely recommended in the USA by the advisory committee on immunization practices (ACIP) to be administered during each pregnancy. The study proves the benefits for both mother and babies, it is expected that future maternal immunizations will have to also obtain a specific indication from the FDA to be administered in this population. In 2014, California experienced a pertussis epidemic with over 11000 reported cases. Young infants have the highest reported rates of illness, hospitalization and death from pertussis. Influenza immunization during pregnancy helps protect both mother and baby from influenza and its complications. Changes to the immune system, heart and lung during pregnancy make pregnant women more susceptible to severe influenza illness, pneumonia, and hospitalization. Collaboration for evaluation of safety profile recommended vaccines in pregnant women and in infants born to vaccinated mothers. Very important for success of immunization and safety of vaccines in pregnant women is the strengthening pharmacovigilence structure. The pharmacovigilence now is almost in every country as part of regulatory agencies or like center of pharmacovigilence, which is necessary to monitor maternal, fetal and newborn and child health.

emkoni@hotmail.com

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COST-EFFECTIVENESS ANALYSIS OF THE INTRODUCTION OF THE PNEUMOCOCCAL CONJUGATE VACCINE (PCV-13) IN THE EGYPTIAN NATIONAL IMMUNIZATION PROGRAM, 2013

Sibak Mohammed
Egypt

Introduction: Pneumonia is one of the most important causes of morbidity and mortality in children under 5 in Egypt, and the Ministry of Health of Egypt is considering introducing pneumococcal conjugate vaccine (PCV) in its national immunization program. We performed an economic analysis to evaluate the cost-effectiveness of this vaccine in Egypt and to provide the decision-makers with needed evidence.

Methods: The analysis was done using the TRIVAC model. Data included demographic characteristics, burden of disease, coverage and efficacy of the vaccine, health resource utilization and costs of pneumococcal disease vaccination and treatment. Whenever possible, we used national or regional data. Two alternatives were compared: (1) general vaccination of children younger than 5 years with the 13-valent pneumococcal conjugate vaccine (PCV13), using a three-dose schedule without booster, and (2) no vaccination. Outcomes of 10 cohorts from birth to 5 years were analyzed. The study was performed from the governmental perspective and selected public health providers.

Results: In comparison to no vaccine, the introduction of PCV13 would be cost-effective, with an incremental cost-effectiveness ratio of US$ 3916 per disability-adjusted life-year (DALY) averted (government perspective). The total incremental cost of the PCV vaccination program (10 cohorts) would be approximately US$ 1.09 billion. Over the 10 cohorts, the program would avert 8583 pneumococcal deaths-42% of all pneumococcal-related deaths.

Conclusion: The introduction of PCV13 would be a good value for money from the government perspective. It would represent a high-impact public health intervention for Egypt and respond to the National Immunization Technical Advisory Group (NITAG) resolution on reducing pneumonia burden and overall child mortality. Strengthening surveillance will be critical in generating high-quality national data, improving future economic analyses that support evidence-based decisions for introducing vaccines and public health interventions, and in monitoring their impact.

sibakmohammed@gmail.com

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PHAGE LYSED BACTERIA AS VACCINES AGAINST PASTEURELLA AND *BRUCELLA* INFECTIONS IN CATTLE

Hari Mohan Saxena, Sabia Qureshi and Sugandha Raj

Guru Angad Dev Veterinary and Animal Sciences University, India

Hemorrhagic Septicemia (HS) is a fatal disease of bovines caused by *Pasteurella multocida*. Marker vaccine could help in control of HS. Bovine brucellosis is an important zoonotic disease causing huge economic losses worldwide. Currently no effective therapy is available for Brucellosis and animals remain carrier lifelong. We have developed novel marker vaccine for HS and therapeutic vaccine for brucellosis employing bacteriophages. *P. multocida* (B: 2) has grown under iron restricted conditions followed by lysis with a lytic *Pasteurella phage* was used as the marker vaccine. Cattle in phage lysate vaccine (PLV) group showed higher antibody titers compared to alum precipitated vaccine (APV) group as revealed by ELISA. Mice and rabbits vaccinated with PLV revealed significantly higher antibody titres than mice and rabbits receiving APV by ELISA (P<0.001). The peak log10 values (3.46) in case of PLV mice by ELISA were attained at 90 days post inoculation (DPI) whereas in APV mice, the peak value at 90 DPI was 2.82. Mean log10 titres by ELISA in PLV and APV rabbits were 2.43 and 2.35, respectively at 30 DPI whereas at 120 DPI, the titres were 3.29 and 2.75, respectively. The marker vaccine induced higher and longer immune response in cattle, mice and rabbits compared to the APV. We have developed a therapeutic vaccine for bovine brucellosis employing phage lysates of RB51 (RL) and S19 (SL) strains of *Brucella abortus*. The SL induced strong antibody response and RL stimulated cell mediated immunity. In vitro restimulation of leukocytes from RL immunized cattle induced interferon gamma production. A single subcutaneous dose of 2 ml of cocktail lysate (both RL and SL), eliminated live virulent *Brucella* from Brucellosis affected cattle. The plasma level of *Brucella* specific 223 bp amplicon became undetectable by RTPCR and blood was negative for live *Brucella* in 3 months post-immunization as evident by culture.

drhmsaxena@gmail.com

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A NOVEL IMMUNOINFORMATICS METHOD FOR SCREENING AND IDENTIFYING SUB MUCOSAL VACCINE CANDIDATES

Neelapu N R R, Pasupuletti A M C, Challa S

Gandhi Institute of Technology and Management (GITAM), India

Several problems were reported with conventional, sub-subunit, inactivated, recombinant and sub-mucosal vaccines. Developing conventional vaccines is labour intensive, expensive and time-consuming. Identifying the most suitable antigens to stimulate the immune system is the limitation with subunit vaccines. The inability to induce cellular immunity is the drawback related to inactivated vaccines and recombinant vaccines. Identifying antibody response for gastric pathogen is the problem with sub-mucosal vaccines. The problem interconnected with specificity of the vaccine is genetic diversity of the pathogen and ethnicity of the patient's population diversity. Therefore, identifying a suitable antigen as a vaccine candidate which can stimulate the immune system, induce cellular immunity, sub-mucosal response against diverse pathogen and population is a challenging task. In this connection, a novel immuno-informatics method is proposed against the above known problems by minimizing the cost of both human and financial resources, without losing efficiency and time. The method includes retrieving the coding regions of the genome and translating them to their respective proteome. Then, the proteome is screened for immuno-pathogenic factors which are non-homologous, non-allergenic, and with helixes≤3. Further, epitopes which are conserved, non-homologous, elicit both T-cell and B-cell response, interact with MHC alleles and IgA antibody, and elicit response in wide range of ethnic populations are identified as suitable antigens. The above approach is a comprehensive immuno-informatics method that enables rapid identification of sub mucosal vaccine candidates with immense potential for therapeutic intervention of pathogens.

nrneelapu@gmail.com

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AN EASY WAY TO ELIMINATE CAUSES OF COLLAGEN AND ALLERGIC DISEASE

Kimihiko Okazaki
Okazaki Medical Clinic, Ukyoku Kyoto Japan

According to the traditional concept of the contemporary immunology, neither autoimmune diseases nor allergic diseases can be cured completely. Nevertheless, a fortunate coincidence led the author to discover a novel concept that eliminations of the causes of these diseases are possible. In other words, combinations of pathogenic antibodies with responsible cells, namely, cytolytic T lymphocytes in cases of autoimmune diseases and mast cells in cases of allergic diseases, can be decomposed by replacing the pathogenic antibodies with non-specific antibodies. In more detail, intradermal injections with a non-specific antigen preparation induce productions of non-specific antibodies in the body of the patient. Repetitions of the injections bring about an accumulation of them. Accumulated non-specific antibodies will occupy most of the receptors on the surface of responsible cells. When the accumulation reaches the sufficient level, virtually no pathogenic antibodies would remain on the receptors. That is, no causes of the diseases remain.

ma13081x@ma1.seikyou.ne.jp

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THE HISTORY OF BIOTECHNOLOGY IN MEDICINE AND IT'S FUTURE PERSPECTIVES

Osama O Ibrahim

Bio Innovation Consulting, USA

Bioprocess technology encompasses all of the basic and applied sciences in microbiology, biochemistry and molecular biology as well as the engineering aspects to fully exploit living systems and bring their products to the market place. Today bioprocesses have become widely used in several fields of commercial biotechnology in medicines, veterinary medicines, food ingredients, agriculture, environmental science and biological chemicals. While our understanding of biotechnological process has rapidly and remarkably advanced in recent years, it has been in existence since prehistoric times, making it one of the oldest technology even before the discovery of microbiology. The term of bioconversion that is also known by the name biotransformation refers to the use of living organisms or its extracted enzymes to carry out chemical reactions that are not feasible or costly when produced by synthetic chemistry methods. These living organisms convert a substance to a chemically modified form with multiple uses and applications. Recent advances in the fields of molecular genetics and nucleic acid chemistry have resulted in a proliferation of biotechnology products. In medicine, modern biotechnology can be used to manufacture existing and new biomedicines relatively easily and cheaply. This modern biotechnology find application in biomedicines such monoclonal antibodies (mAbs), therapeutic proteins, pharmacogenomics, and genetic testing.

Bioinnovation04@yahoo.com

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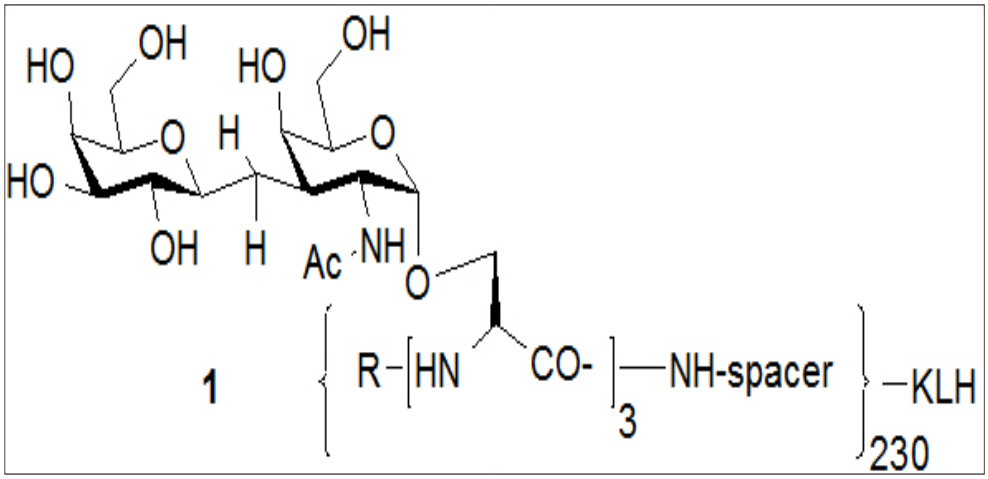
DISACCHARIDE MIMETICS AS DRUGS AGAINST CANCER AND EPITOPES FOR ANTI-CANCER VACCINE CANDIDATES

Loay Awad and Pierre Vogel

Swiss Institute of Technology in Lausanne (EPFL), Switzerland

Cancer-associated mucin glycoprotein MUC1 is characterized by the presence of altered carbohydrates such as Tn (α-N-acetylgalactosamine), sTn (sialyl-1-6-Tn) and the Thomsen-Friedenreich (TF: β-D-Galp-1-3-α-D-GalNAcp) antigen (tumor associated carbohydrate antigens: TACAs) that are conjugated to proteins via O-α-galactosylation of serine or/and threonine. Patients immunized with synthetic TF conjugated with KLH (keyhole limpet hemocyanin) + QS21 adjuvant can generate IgM and IgG antibodies because, the disaccharide TF is hydrolyzed rapidly in the body, strong immune response requires longer lived disaccharides. Fluororinated TACAs have been proposed which elicit IgG antibodies found to cross-react with native TF epitopes. We have found that the C-linked disaccharide analogue 1 (constructed applying Danishesky's method for the conjugation with KLH) + QS21 adjuvant induces a strong immune response in mice. Interestingly, much weaker immune response was observed with a stereoisomeric antigen constructed with the α-C-galactoside analogue of TF disaccharide (α-D-Galp-1-CH2-3-α-D-GalNAc-O-Ser). Several strategies and methods have been developed for the synthesis of C-linked disaccharides including disaccharide mimetics incorporating iminosugars C-linked to sugars and sugar mimetics such as conduritols and cyclitols. The latter work was motivated by the search for specific glycosidase and glycosyltransferase inhibitors that are potential drugs against cancers and other diseases.

Pierre.vogel@epfl.ch



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EVIDENCE-BASED RECOMMENDATIONS FOR THE PREVENTION OF POSSIBLE HEPATITIS A VIRUS (HAV) EPIDEMICS IN EUROPE

Sami Ramia
Lebanon

Introduction: Europe and other Western countries are considered to be areas of low endemicity of Hepatitis A infection, thanks to relatively good hygienic and sanitary conditions. However, due to the large influx of refugees to Europe from Middle East and North Africa regions, which are highly endemic for hepatitis A, several Hepatitis A outbreaks have been recently reported. Moreover, several HAV infection outbreaks have also been recently reported in Europe among men who have sex with men (MSM).

Materials/methods: We performed a systematic PubMed and Medline search to identify published studies on HAV epidemiology and/or outbreaks in European countries during the past 5 years.

Results & Discussion: Since the start of the refugee crisis in Europe in 2015, there were 2 major studies in Europe on HAV infection among refugees: one was in Greece and the other one was in Germany. The one in Greece reported 177 HAV cases among 62,700 refugees coming from the conflict zone particularly from Syria, Iraq, and Afghanistan. During the same period of time, 4 HAV cases were detected between staff responsible for cleaning in 2 hosting camps. In Germany, 699 HAV cases have been reported between Sep' 2015 and Mar' 2016 compared to 482 cases in the same period of previous year. One case has been reported at a nurse working in a mass accommodation. Other studies deduced that the most frequent risk factor to generate new cases of HAV is an immigrant making a recent trip to the country of origin where the endemicity of disease is high. Moreover, hepatitis A outbreaks have been recently reported among men who have sex with men (MSM) in different European countries including Italy, Spain, the Netherland, and England. In the light of these new studies, evidence-based recommendations for the prevention of possible HAV epidemics in Europe are being advanced.

sramia@aub.edu.lb

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IMMUNOLOGICAL STUDIES ON TETANUS TOXOID

Rakesh Kumar
Serum Institute of India Limited, India

Tetanus toxoid is one of the most successful vaccines used in immunization programme almost all over the world. Neonatal tetanus can be prevented by immunizing women of childbearing age with tetanus toxoid, either during pregnancy or outside of pregnancy. Tetanus vaccine is used either in mono or in combination with other antigens i.e. Diphtheria, Pertussis (whole cell or a cellular), Hepatitis B, Haemophilus influenza B, Inactivated polio vaccine etc. Tetanus toxoid is produced batch-wise using complex media, often containing poorly defined components. Therefore, batch related quality control to guarantee safety and potency is a statutory requirement. In the new concept, quality control is seen as an instrument to monitor consistency of the critical steps in the production process and testing of vaccines. Monitoring consistency places emphasis on in-vitro methods, since in-vivo tests are less appropriates (expensive, time consuming and inaccurate) for this purpose. Immunochemical techniques may include the use of polyclonal antibodies for direct ELISA or monoclonal antibodies in capture ELISA and immunoblotting to indicate local differences in antigenicity. There is no uniformity in the potency test of tetanus toxoid. Potency assays in animals may be seen as a way of estimating relative antigen contents parallel to the in-vitro estimations; e.g. by the flocculation tests or the Mancini test. In animal tests, however, it is the ability to provoke production of antibodies (immunogenicity) that is utilized and not just the ability to react with antibodies (antigenicity). This distinction might be carried even further. In challenge tests, the ability to create protection against toxin challenge is the reaction used (protective immunogenicity). In antibody production assays the ability to provoke production of antibodies reacting in a certain antibody detection system is used. In the past, the potency of tetanus toxoid was being expressed in Lf - units. United States Pharmacopoeia prescribed antibody induction method. British Pharmacopoeia, other European countries and World Health Organization recommended active challenge method for assaying the potency of tetanus component. However, Indian Pharmacopoeia prescribed both the methods viz. antibody titration method and active challenge method. For the potency estimation of tetanus toxoid component in mono-valent or combination vaccines, the challenge test has been in use for many years. Despite the use of large number of animals (> 100 mice or guinea pigs) to test one batch of tetanus toxoid, this test has not been shown to correlate with immunogenicity in humans. However, toxin-neutralizing antibodies induced by the vaccine are generally accepted as correlates of protection. The three 'R's concept for the replacement, reduction and refinement of the use of laboratory animal testing is now widely accepted as not only need for ethical but also for scientific reasons.

This study on immunogenicity of tetanus toxoid is focused on the following parameters to analyse and evaluate the quality of toxoid:

- Comparative study of active challenge method and direct ELISA method for assaying the immunogenicity.
- Comparative study of active challenge method and capture ELISA method for assaying the immunogenicity.
- Comparative study on potency by active challenge method and antibody induction method.

rakesh.kumar@seruminstitute.com

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TO INVESTIGATE IF OTHER STIS CONTRIBUTE TO HIV TRANSMISSION

Salim Slim
Dhiverse, UK

Methods: We collected data from ten RTCs conducted in between 1990-2010, analysed these data and the study design. We use static model approach to analyse the data from these trials and assess these trials by reviewing their study designs to identify the limitation and strength of each trials.

Results: Only the first study of ten studies show statistical significant on the effect of other sexually transmitted infections (STIs) on HIV transmission. Results from the rest of nine studies showed very weak or no evidence the effect of STIs on HIV transmission. Mathematical model data suggested 64% reduction if STIs syndromic management were introduce at early phase of the epidemic, the delayed STIs management show only 5.5% HIV reduction in South Africa.

Studies analysis and limitation: Phase of HIV epidemic, study design and clinical equipoise collectively play major role in the outcome of these studies which cause masking of the true effect of STIs on HIV transmission on both by facilitating both infectiousness and susceptibility.

Conclusion: HIV continues to pose major health challenges. Trials in these studies have shown unsatisfactory results and create confusion between HIV scientific communities. The analysis of these trials has clearly demonstrated the flaws within the studies which resulted in masking the true magnitude of STIs on the transmission of HIV. However, the mathematical modelling studies and biological plausibility mechanism consistence indicated that presence of STIs mostly ulcerative such as syphilis and chancroid contribute to 40% of HIV transmission in SSA. Any efforts aiming to achieve effective HIV prevention without effective STIs management are most likely to be weakened. The lack of evidence in these RCTs should not conclude lack effectiveness.

Recommendation: STIs management including vaccination will enhance the effort of shrinking HIV epidemic.

salimslim@icloud.com

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TOWARDS SEVERAL BIOLOGICAL ACTIVITIES COMPOUNDS

S Chtiba[1,2], H Tazarki[1,4], I Amri[3,4], J Khiari[1] and J Bassem[1]

[1]Institut Supérieur de l'Education et de la Formation Continue, Tunisia
[2]Faculté des Sciences de Tunis (FST), Tunisia
[3]Institut national de recherches en génie rural, Eaux et Forêts (INGREF), Tunisia
[4]University of Carthage, Tunisia

Fused heterocyclic containing pyrazolopyridine systems have been described associated with several biological and medicinal activities. So, in this study, we described firstly an expedient method for the synthesis of substituted pyrazolo [3,4-b]pyridines derivatives in a single-step according to our recent study with synthesis strategy amelioration. Then, we screened for antibacterial effects against respectively Bacteria (Escherichia coli CIP 53126 and *Bacillus subtilis* CIP 5262) and Fungi (*Candida albicans* ATCC 10231 and *Aspergillus Niger* ATCC 16404). Hence, according to the antimicrobial activity results, some of these compounds have similar or higher activity compared with commercial antibiotic drugs (Spiramycin, Streptomycin and Fluconazol), which make them suitable for diverse applications like the manufacturing of drugs, pesticides. In the other hand, their total inhibition against *Aspergillus Niger* provides evidence that these pyrazole formulations could be an alternative source for the treatment of fungal infections caused by *Aspergillus Niger* ATCC 16404.

samarchtiba@yahoo.com

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VACCINE AGAINST DIABETES: IS THERE A POSSIBILITY

Venkataramana Kandi[1], Sabitha Vadakedath[2]

[1]Prathima Institute of Medical Sciences, India
[2]Chalmeda Anandrao Institute of Medical Sciences, India

Diabetes mellitus is a chronic debilitating non-communicable disease prevalent throughout the world. There are two different types of diabetes; the type 1 diabetes usually presents in children and young adults, and the type 2 diabetes, a most frequent age-related condition usually noted among the adults aged over 40 years. The type 1 diabetes results due to an immunological reaction against insulin and the insulin secreting cells. The type 2 diabetes can occur due to various factors that include genetic predisposition, lifestyle disorders, insulin resistance, and lack of adequate insulin production. Since lifestyle management is an adjustable risk factor for diabetes, may people with genetic predisposition could delay the onset of clinical diabetes. Further, there is an increasing need to understand the genetics behind the signalling pathways involved in the development of type 2 diabetes which could pave the way for formulating and implementing therapeutic and preventive strategies. The genetic reasons for the development of T2DM involve a complex interlinked signalling cascade. There are several genes which influence post translational modifications (ARAP1, ADCY5, SPRY2, FTO), some genes related to metabolism (RBMS, HNF4A, HNF1A, PROX1, PPARG, GCKR), some involved in the development of pancreas (GLIS, HNF1B, HHEX, IGF2BP2), and a few are related to insulin secretion (GRB14, CDKAL1, ZBED3, GIPR). There are also some genes (SLC30A8) involved in insulin storage, glycosylation (ST6GAL1), apoptosis (THADA), cancer (BCL11A), metal related gene (NOTCH2), and drug related genes (KCNJ11).

ramana200221@gmail.com

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EXPLORING SAND FLY SALIVARY PROTEINS TO DESIGN MULTI-EPITOPE BASED SUBUNIT VACCINE TO FIGHT AGAINST VISCERAL LEISHMANIASIS

Vijay Kumar Prajapati
Central University of Rajasthan, India

Background: Visceral leishmaniasis (VL) is a serious public health issue which causes >30,000 death/year in 70 countries. Here, we have explored sandfly salivary proteins and followed comprehensive immunoinformatics approach to design multi-epitope subunit vaccine which may elucidate humoral, cell mediated and innate immune responses.

Methodology: Sandfly salivary proteins were employed for prediction of B cell and T cell binding epitopes. TLR4 agonist 50S ribosomal L7/L12 (Locus RL7_MYCTU) was chosen as adjuvant at the N-terminal followed by CTL and HTL epitopes. This vaccine construct was studied for investigating B cell binding and IFN-γ inducing epitopes. This was followed by prediction of antigenicity, allergic nature and physiochemical properties of the vaccine construct after which generation, refinement and validation of the vaccine model were performed. The interactions of this vaccine model with its immune receptor were explored by performing molecular docking and molecular dynamics simulation. Further, efficiency of expression of this vaccine construct in an expression vector, in silico cloning was performed at the final stage of vaccine design.

Result: The multi-epitope subunit vaccine construct consist of 8 CTL and 15 HTL epitopes. Final 903 amino acids vaccine constructs have shown B cell epitopes (humoral response) and INF-γ epitopes (cell mediated immune response). Vaccine construct was found to be non-allergen, antigenic and valid 3D protein structure was confirmed by Ramachandran plot. Molecular docking and dynamics simulation experiments have shown significant interaction with the TLR4 receptor present on the surface of immune cells. Wrangler and gene synthesis wizard and GeneScript rare codon analysis have shown good expression of vaccine construct in E. coli.

Conclusion: Applied comprehensive immunoinformatics approaches have designed a multi-epitope subunit vaccine, which necessitates experimental and clinical investigation to develop as an immunogenic vaccine candidate to prevent VL infection.

vkprajapati@curaj.ac.in

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VACCINATION CAMPAIGN IN JORDAN VERSUS BROKEN PRIMARY HEALTH CARE CENTRES

Zeyad S Bataineh, Sameer Kofahi
King Hussein Medical Center (KHMC), Jordan

Statement of the problem: New cases of polio, measles and rubella began to appear in the Mediterranean region, including Jordan due to breakdown of primary health care system and a lot of children in Syria were definitely infected with these major diseases caused by the civil war. World Health Organization (WHO) adopted a vaccination campaigns in neighbouring countries closed to Syria since 2nd Nov' 2015 to 21st Nov' 2015 in order to control the spread of the disease through the reservoir (refugees) getaway from Syria to neighbouring countries such as Jordan.

Objective: Control, prevention and eradication of polio, measles and rubella.

Method: A vaccination campaign for these major diseases (polio, measles and rubella) in the period of 2nd Nov to 21st Nov' 2015 carried out this campaign through the Ministry of Health Jordan (MOH), Royal Medical Services (RMS), United Nations Relief and Works Agency (UNRWA) and non-governmental organizations (NGOs) health centres across the Jordan.

Target population: The campaign targets the vaccination children against polio for the age group of one day to five years, while the targeted immunization with vaccine of measles and rubella for the age group of 6 months to 20 years for all Jordanians and non-Jordanians residing on the land of the Kingdom regardless of taking them to these vaccines earlier in the campaign.

Result: Total number of children and young people within the age group of the day and until the age of 20 years had vaccination (2,500000), among of those (56500) vaccinate by RMS as well as about (46000) measles and rubella, (10500) polio vaccine.

Conclusion: High vaccination coverage as well as a huge number of people from under the age of 20 years attended Ministry of Health, Royal Medical Services, UNRWA, and non-governmental organizations health care centre in Jordan to get vaccination.

Zeyad7620@yahoo.com