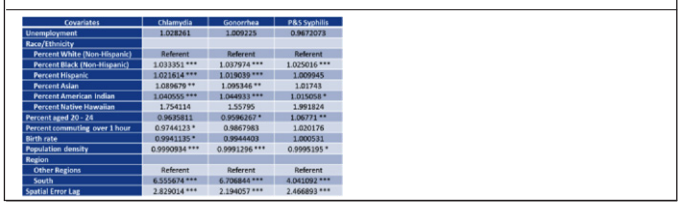


Covariates	Chlamydia	Gonorrhea	P&S Syphilis
Unemployment	1.028261	1.009229	0.9673073
Race/Ethnicity			
Percent White (Non-Hispanic)	Referent	Referent	Referent
Percent Black (Non-Hispanic)	1.033351 ***	1.037974 ***	1.025016 ***
Percent Hispanic	1.021614 ***	1.018039 ***	1.009945
Percent Asian	1.089679 **	1.095346 **	1.01743
Percent American Indian	1.040555 ***	1.044933 ***	1.015058 *
Percent Native Hawaiian	1.754114	1.55795	1.991824
Percent aged 20 - 24	0.9635811	0.9596267 *	1.06771 **
Percent commuting over 1 hour	0.9744123 *	0.9867983	1.020176
Birth rate	0.9941135 *	0.9944403	1.000531
Population density	0.9990934 ***	0.9991296 ***	0.9995195 *
Region			
Other Regions	Referent	Referent	Referent
South	6.555674 ***	6.706844 ***	4.041092 ***
Spatial Error Lag	2.829014 ***	2.194057 ***	2.466893 ***

6.6 ($p < 0.01$; chlamydia), 6.7 ($p < 0.01$; gonorrhea) and 4.0 ($p < 0.01$; P&S syphilis) times more likely to be hot spots (Table 1).

Conclusion: Our study provides important information on hot spot clusters of non-viral STIs in the entire US, including associations between hot spot counties and socio-economic/demographic factors.

http://dx.doi.org/10.1016/j.ijid.2016.02.139

Type: Oral Presentation

Final Abstract Number: 28.003
Session: Oral Presentations: Bacterial Infections & Vaccines
Date: Friday, March 4, 2016
Time: 15:45-17:45
Room: G.05-06

Recombinant accessory cholera enterotoxin of Vibrio cholerae activate ANO6 via RhoA-ROCK-PIP2 signaling to induce secretary diarrhea

I.A. Sheikh [1,*], J. Aoun [2], P. Sarkar [3], T. Saha [2], M.H. Kazi [2]

[1] *National Institute of Cholera & Enteric Diseases, Kolkata, West Bengal, India*
[2] *National Institute of Cholera & Enteric Diseases, Kolkata, India*
[3] *National Institute of Cholera and Enteric Diseases, Kolkata, West Bengal, India*

Background: *Vibrio cholerae* accessory cholera enterotoxin (ACE) is the third toxin alone with cholera toxin and zonula occludens toxin that cause secretary diarrhea by activating Ca^{2+}-dependent Cl^-/HCO_3^- symporters. However, the identity of the underlying signalosomes and Cl^- channel specifically activated by ACE is unknown because of the low amount of toxin produced by *V. cholerae*.

Methods & Materials: Using previously established biologically active recombinant ACE, Ussing chamber and patch clamp techniques, we examine the identity of unknown apical Cl^- channel activated by ACE to cause diarrhea.

Results: We observed ACE induce apical Cl conductance (ICl^-) sensitive to classical calcium activated Cl channel (CaCC) blockers such as NPPB, niflumic acid, and AO1 but was neither affected by ANO1 (TMEM16A) specific inhibitor T16A-AO1 nor by CFTR blocker, CFTRinh-172. In vivo mice ileal loop experiment reveal similar sensitivity of ACE induced fluid accumulation in presence of various CaCC inhibitors. Based on these pharmacological studies, we hypothesized ACE activated CaCC ANO6 (TMEM16F) to induce apical Cl^- secretion. This hypothesis validated by robust ANO6 expression in intestinal epithelial cell model Caco2 cell line and reduced ICl in ANO6 knockdown Caco2 cell relative to wild type ings of Cl^- currents upon ACE exposure in HEK293 cells transiently expressing ANO6-GFP but not ANO1-mCherry. However, treatment with calcium ionophore A23187 induced strong outwardly rectifying ANO1 and ANO6 currents in these HEK 293 cells. Surprisingly, ACE was not able to induce $[Ca^{2+}]i$ rise in these cells. Together, these data indicate ACE elicits whole cell Cl^- currents by calcium-independent mechanism of ANO6 activation by ACE. Further investigation reveal Caco2 cells expose to ACE cause significant RhoA translocation to plasma membrane while ACE evoke ICl^- decreases in presence of RhoA kinase (ROCK) inhibitor, H1152 and PI4K inhibitor, wortmannin and PAO which reduces plasma membrane PIP2 level. We have also identify PIP2 binding motif at the N-terminal sequence among human and mouse ANO6 variants.

Conclusion: We conclude increased plasma membrane PIP2 level via RhoA-ROCK-PIP2 signaling cascade induced specific activation of ANO6 by during ACE mediated secretary diarrhea.

http://dx.doi.org/10.1016/j.ijid.2016.02.140

Type: Oral Presentation

Final Abstract Number: 28.004
Session: Oral Presentations: Bacterial Infections & Vaccines
Date: Friday, March 4, 2016
Time: 15:45-17:45
Room: G.05-06

A decade of antimicrobial stewardship at the University of Florida - Challenges, strategies and outcomes

K. cherabuddi [1,*], K. Klinker [2]

[1] *University of Florida, Gainesville, FL, USA*
[2] *University of Florida, Gainesville, USA*

Background: Antimicrobial Management Teams (AMT) play an integral role in modifying antimicrobial utilization (AU). In 2004, AMT at Shands UF developed restricted antimicrobial policy (RAP) with institutional criteria for carbapenems (CAR), piperacillin/tazobactam (P/T), daptomycin (DAP), echinocandins (EC), cefepime (CEF) and fluoroquinolones (FQ). In 2008, AMT was disassembled due to pharmacist attrition but RAP remained under Infectious Diseases (ID). AMT was re-initiated in 2010 and later further expanded. We report the experience of the AMT over a 10-year period and the impact on consumption, resistance, drug costs and various oppurtunities, challenges and strategies.

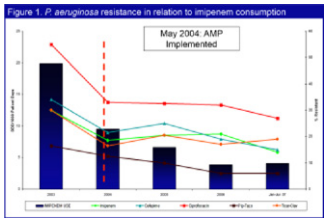
Methods & Materials: A retrospective evaluation was performed to compare the consumption of targeted antimicrobials, measured as defined daily dose per 1000 patient days, before and after AU management strategies were initiated and also when AMT was disassembled and again when it was re-initiated. AU, Acquisition costs (AC) and Resistance rates (RR) from 2003 were compared to 2006/7 and also from 2008 was compared to 2010. Following re-implementation, AMT's central role focused on RAP adherence with direct prescriber feedback on Days 3 and 7 of therapy.

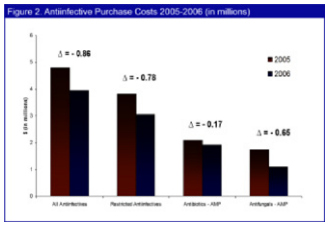
Results: With Initiation of AMT in 2004, consumption of most anti-pseudomonal antibiotics fell: IMI (-80%), P/T (-22%), T/C (-60%), CEF (-3.8%) and FQs (-37%). Resistance among *Pseudmonas* to targeted antibiotics has stabilized and displays a downward trend. Antimicrobial drug acquisition costs decreased by 18%.

Following loss of AMT, antimicrobial expenditure (AE) and antibiotic cost per patient day (ACPD) increased by 33 and 22% respectively. Increased consumption of aztreonam (78%), CEF (6%),

EC (25%), FQ (20%), CAR (4%), and DAP (133%) occured. In 2010, AMT was re-implemented and resulted in 12 and 15% reduction in total AE. Cost savings exceeded $300,000.

From 2010 to 2014, we have implemented multiple strategies to further control AU.





Conclusion: Since 2004, AMT has implemented strategies that reduced the consumption of RAP agents and *Pseudmonas* resistance has not increased. Re-implementation of AMT responsible for administering institutional guidelines and providing direct feedback resulted in rapid decrease in AE, ACPD. The most gains in the AMT implementation occur early and sustaining an effective AMT requires administrative support and adapting strategies to challenges faced and anticipated.

http://dx.doi.org/10.1016/j.ijid.2016.02.141

Type: Oral Presentation

Final Abstract Number: 28.005
Session: Oral Presentations: Bacterial Infections & Vaccines
Date: Friday, March 4, 2016
Time: 15:45-17:45
Room: G.05-06

Guillain–Barré syndrome in Bangladesh: The role TLR4 Asp299Gly and Thr399Ile polymorphisms

I. Jahan [1], R.U. Ahammad [1], M.M. Khalid [1], S.K. Sarker [1], M.B. Islam [1], H.P. Endtz [2], Z. Islam [1,*]

[1] *International Centre for Diarrhoeal Disease Research, (icddr,b), Dhaka, Bangladesh, Dhaka, Bangladesh*
[2] *Erasmus University Medical Centre, Rotterdam, The Netherlands, Rotterdam, Netherlands*

Background: Bangladesh has achieved a remarkable success to eradicate poliomyelitis, however, Guillain–Barré syndrome (GBS) is frequently diagnosed. GBS is an autoimmune mediated disease of the peripheral nervous system preceded by infections. *Campylobacter jejuni* has been identified as the predominant cause of antecedent infection in GBS. *C. jejuni* lipopolysaccharide (LPS) induces antibodies cross-reactive with gangliosides and has shown to be involved in peripheral nerve damage. Toll-like receptor 4 (TLR4) is an important pathogen recognition receptor that recognizes mainly lipopolysaccharide (LPS) of gram-negative bacteria. In this study, we investigated functional single nucleotide polymorphisms (SNPs) in the extracellular domain of TLR4 (Asp299Gly and Thr399Ile), and assessed their association for GBS susceptibility, disease pathogenesis and disease outcome.

Methods & Materials: A hospital based case controlled study was conducted in Dhaka Medical College Hospital (DMCH) in Dhaka, Bangladesh in between 2010 to 2013. A total of 210 genomic DNA (105 consecutive patients with GBS and 105 healthy controls of Bangladeshi population) were isolated using QIAGEN (DNA) blood midi kit and genotyped by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

Results: TLR4 (Asp299Gly) polymorphism were significantly associated with GBS patients compared with healthy controls ($p < 0.05$). Gly299Gly homozygote increased the susceptibility of GBS patients compared with healthy controls ($p = 0.0365$, OR = 8.9, 95% CI = 1.1-73.2). Acute motor axonal neuropathy (AMAN) was significantly associated with Gly299Gly homozygote (p=0.0093, OR=14.6, 95% CI = 1.6-130.7). TLR4 variant genotype Asp/Gly ($p = 0.0441$, OR = 2.6, 95% CI = 1.1-6.5) was associated with poor outcome (unable to walk after 6 months); suggesting that these genotype might be one of the factors contributing to a severe form of GBS. No significant association of TLR4 polymorphism (Asp299Gly and Thr399Ile) with anti-ganglioside antibodies was found. In addition, TLR4 Thr399Ile polymorphism had no role in GBS susceptibility as compared with controls.

Conclusion: TLR4 Gly299Gly homozygote is associated with the increased disease susceptibility to GBS. Gly299Gly homozygote is also associated with the axonal variant of GBS. However, TLR4 Asp299Gly polymorphism is prevalently significant with the disease outcome of GBS. Therefore, further study is required to confirm this association using a large cohort.

http://dx.doi.org/10.1016/j.ijid.2016.02.142

Type: Oral Presentation

Final Abstract Number: 28.006
Session: Oral Presentations: Bacterial Infections & Vaccines
Date: Friday, March 4, 2016
Time: 15:45-17:45
Room: G.05-06

Identification of biofilm-stage specific proteins associated with multidrug resistance and quorum sensing pathway in a pandemic strain of Vibrio parahaemolyticus isolated from India

A. Dharmaprakash*, S. Thomas

Rajiv Gandhi Center for Biotechnology, Thiruvananthapuram, Tamil nadu, India

Background: *Vibrio parahaemolyticus*, a Gram negative halophilic bacterium, is rated as one of the leading etiological agent of food borne diseases in humans. Gastroenteritis is the most common clinical manifestation and specific serotypes of this pathogen were associated with pandemic outbreaks in several parts of the world since 1996. Recent studies conducted in the related Vibrio pathogens has revealed the role of biofilm mode of life in the emergence of multidrug resistance and pathogenicity. Present study was conducted to identify the genes and pathways specific to the biofilm stage of *V. parahaemolyticus* employing high throughput global proteomic approaches.