P1-Ab0009

A randomized, controlled clinical trial: The effects of mindfulness-based cognitive therapy on generalized anxiety disorder and health service utilization in primary care

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Background: Generalized anxiety disorder (GAD) is one of the most common mental health problems seen in the primary care or community setting. Research suggests that an eight-week mindfulness based cognitive therapy (MBCT) may be effective in the treatment of GAD.

Objectives: This three-armed randomized controlled clinical trial aimed to evaluate the effectiveness of MBCT in reducing anxiety symptoms among patients with GAD.

Methods: A total of 182 participants with GAD who scored 19 or above in the Beck Anxiety Inventory were randomly assigned to the MBCT, psycho-education group (PEG) or usual care control group (UC). Anxiety and worry symptoms as well as depressive symptom, quality of life and health utilization were assessed using validated Chinese version of instrument at baseline, immediately and three months after intervention for all three groups. The MBCT and PEG group were further followed up at six and nine months after the intervention.

Results: Participants from both MBCT and PEG group had significant decrease on anxiety symptoms as compared to the UC group at immediately (MBCT vs. UC, $p = 0.014$; PEG vs. UC, $p = 0.002$) and 3 months after the intervention (MBCT vs. UC, $p = 0.001$; PEG vs. UC, $p < 0.001$).

Conclusions: People suffering from GAD may benefit from both MBCT or PEG in reducing their anxiety. PEG, however, may be a better approach and intervention for the reduction on depressive symptoms and quality of life although the lack of significant findings on these measures in the MBCT group could also be due to the higher non-compliance rate for mindfulness practice.

Ref. No.: 07080451

P2-Ab0015

Prevention of Anxiety and Depression in Chinese: A Randomized Clinical Trial Testing the Feasibility and Effectiveness of a Generic Stepped Care Programme in Primary Care

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Background: Subthreshold depression and anxiety are found to be prevalent in primary care. Indicated prevention using stepped care approach targeting those at high risk of depression and anxiety is needed.

Objectives: To test the effectiveness of a stepped care model to prevent the onset of anxiety and depressive disorders in people with subthreshold anxiety and depression when compared to usual care.

Methods: A total of 240 participants in primary care with subthreshold depression and/or anxiety were recruited in and randomly assigned to the stepped care or usual care group. Measurements were conducted at baseline, 3, 6, 9, 12 and 15 months. The primary outcome was the incidence of depression and/or anxiety disorders at 1 year. Secondary outcomes included the change in scores of the Center for Epidemiologic Studies Depression Scale (CES-D), Hospital Anxiety and Depression Scale (HADS) Anxiety Score (AS), Beck Anxiety and Depression Inventory, health care utilisation and quality of life (SF-12).

Results: Twenty-one participants from the stepped care group and 18 from the care as usual group developed depression and/or anxiety disorder at 15 months. The probability of developing depression and/or anxiety disorders was 13.53% at 12 months (14.2% for the stepped care group and 12.7% for the care as usual group) and 21.81% at 15 months (23.1% for the stepped care group and 20.5% for the care as usual group). No significant differences were found in the stepped care group in decreasing incidence using Cox proportional hazards model (HR = 1.62, 95% CI: 0.82-3.18, P = 0.16) and symptoms of depression and/or anxiety and health care utilisation and improving quality of life using mixed models (P-values > 0.05).

Conclusions: The stepped care programme did not show beneficial effect in preventing onset of depression and/or anxiety, reducing severity of symptoms and health care utilisation, and improving quality of life among primary care patients with subthreshold depression and/or anxiety compared with care as usual at 15 months.

Ref. No.: SMH-03

P3-Ab0139

15-year Computer Case Record Follow-up Study on Adolescents with Previous Exposure to Peers' Suicide

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Introduction: In 94/95, we conducted a study on the peers of Chinese adolescent suicide attempters and completers in Hong Kong and found that both represented high risk group for psychiatric disturbances and suicidal behaviors. Close friends of suicide completers were at risk of internalizing problems whereas close friends of suicide attempters were at risk of externalizing problems.

Objectives: The current study is a territory-wide computer record-linkage study on this cohort to examine whether previous exposure to peers' suicide is associated with more psychopathology,

contacts with Accident and Emergency Department(AED) and/or psychiatric services.

Methods: The subjects were drawn from an existing database compiled 15 years ago when they (from both target and control schools) were administered a standardized questionnaire on their own and previous exposure to suicidal behavior. 3 groups were formed: peers of suicide attempters, peers of suicide completers and non-exposed controls.

2701 out of the original database of 2869 subjects could be used for this current research. Data was retrieved from the Clinical Management System of the Hospital Authority(HA) on specific outcome variables in terms of psychopathology, attendance at AED and psychiatric clinics/hospitals within HA.

Results: Female subjects exposed to completed suicide attend more AED than female non-exposed controls; 44.3% (120/271) of the former attended AED thrice or more vs. 35.3%(213/604) of the latter (X2=8.147, p=.017). Similarly female subjects exposed to attempted suicide attend more AED than controls; 42.4% (225/531) vs. 35.3% (213/604); (X2=6.117, p=.047). Male subjects showed similar trends, though the effect sizes were smaller and statistically insignificant. 40.4% (113/280) of males exposed to completed suicide attended AED thrice or more vs. 35.5% (270/761) of controls (X2= 2.396, p =.302). 38.6% (98/254) of males exposed to attempted suicide attended AED thrice or more vs. 35.5% (270/761) of control (X2=0.809, p =.667). No significant difference was found among the exposed and non-exposed groups on the number of contacts with psychiatric services, self-harm, suicidal behavior, death, AED's diagnoses, drug abuse, aggressive behavior, and psychiatric diagnoses.

Conclusions: The data showed that after 15 years, there was no significant group difference, except for AED attendance for female subjects (and to a lesser extent for male subjects), between those who were exposed to completed or attempted suicides and the non-exposed controls. The difference in AED attendance poses an interesting research question whether the exposed subjects possess a different type of help-seeking behavior that warrants further research.

Ref. No.: SMH-37

P4-Ab0144

Telephone-assisted Pleasant Event Scheduling (TAPES) for Enhancing the Well-being of Dementia Caregivers

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This pilot study examined the effectiveness of Telephone-Assisted Pleasant Event Scheduling (TAPES) targeted to enhance the psychological well-being of dementia caregivers. Sixty dementia caregivers were randomized to the TAPES intervention or the treatment as usual (TAU) group. Over 4 weeks of intervention, participants in the TAPES group were systematically guided to develop an individualized plan of schedule pleasant events with subsequent implementation. The treatment rationale in terms of behavioral activation and adpative coping was also discussed. Analysis of covariance was used to compare the TAPES and TAU group. The TAPES group was found to have significantly lower levels of depressive symptoms than the TAU group. Treatment gains were maintained at one-month follow-up. Findings suggested that a short-term telephone-assisted intervention program

employing behavioral activation procedures was successful in improving the mood of dementia caregivers. These findings highlight the potential of time-limited and telephone-assisted intervention as an effective model of care to enhance accessibility and overcome barriers of care for dementia caregivers. Pleasant event scheduling can have special significance in the Chinese culture which underscores coping flexibility.

Ref. No.: 08091141

P5-Ab0128

Medium and Long-term Follow Up of Children with History of Melamine Exposure in Hong Kong: A Multicentre Study

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Background: In 2008 an outbreak of acute renal conditions in children was linked to high dose melamine exposure. Reports on severely affected children in the Chinese Mainland focused on high dose exposure. Hong Kong children were exposed to levels near the World Health Organization tolerated daily intake of 0.2 mg/kg. Data regarding outcomes of low dose melamine exposure in children is thus needed.

Aims: A multi-centre study to investigate the medium to long-term renal outcomes of children with a history of melamine exposure in Hong Kong.

Study Design: Children screened at the special assessment centres in Hong Kong were invited to return for follow up if they were found to have either (i) ultrasound evidence of renal stones, deposits or obstruction, or (ii) abnormalities on urine reagent strip testing. Eligible children were prioritised for recruitment according to: (i) estimated melamine intake, (ii) clinical features of renal disease, and (iii) young age. All subjects received serial renal ultrasonography, urinalysis, urine beta-2-microglobulin measurement and creatinine clearance estimation (from spot plasma creatinine). In addition those with ultrasound abnormalities received further investigations for causes of renal stones.

Results: 62 subjects with ultrasound abnormalities and 321 subjects with urine abnormalities were recruited. No clinically significant differences were found between children exceeding World Health Organization melamine tolerable daily intake levels (0.2 mg/kg body weight) and those who did not in either study group. Renal function parameters were normal in all subjects. Renal outcomes were not associated with estimated melamine intake at the low levels found in Hong Kong.

Conclusions: No associations between estimated melamine exposure and medium to long-term adverse renal outcomes were found in our study.

Implications: Our study does not provide evidence to support routine follow up for asymptomatic children with a history of low dose melamine exposure.

Ref. No.: MI-FU-01

P6-Ab0026
Impact of Cognitive and Emotional Illness Representations on Stigma and Recovery

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Background: Common sense model hypothesized that individuals' mental representations of illness can influence the way they appraise and manage their illness. Prior investigations showed that negative perception towards their illness was associated with poor mental well-being as well as impaired role and social functioning. This study aimed to examine how cognitive and emotional illness representations among people in recovery might affect their stigma associated with mental illness and recovery.

Methods: A cross-sectional survey was administered to 374 people in recovery of mental illness (24.1% with schizophrenia spectrum disorders, 42.8% with mood disorders; 33.2% with substance abuse; 49.9% female; mean age = 43.47, SD = 12.76) in Hong Kong. They were asked to assess the perception towards their illness, self-stigma, symptom severity, and personal recovery. Structural equation modelling was conducted to examine how illness representation of people in recovery can affect their self-stigma and influence their recovery outcomes.

Results: Results indicated that a satisfactory fit of the hypothesized model, $\chi2(106) = 353.30$, $p<.001$, CFI = .91, RMSEA = .08. Illness perceptions explained 21.2% variance of self-stigma and self-stigma in turn explained 24.8% and 28.8% variance of personal and clinical recovery, respectively. Specifically, people who viewed their mental illness as having long-term negative consequences, felt less control over their illness, could recognize their symptoms, and had negative emotional reactions towards their mental illness were more likely to report self-stigma, which dampened their recovery outcomes.

Conclusions: This study demonstrated that the way that people in recovery make sense of their illness can influence their construction of self-stigma of mental illness, thereby shaping their personal and clinical recovery. Psychoeducational interventions aimed at empowering individuals to take control of their mental illness and their lives and restructuring their maladaptive illness-related beliefs and regulating their emotions are recommended.

Ref. No.: SMH-14

P7-Ab0027
Infant Growth and Pubertal Adiposity Associations: Implications to Future Cardiovascular Health and Immunological Benefits

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Introduction: Cardiovascular disease is the leading cause of death. Influences throughout life affect long-term health. Infancy is potentially key window of developmental plasticity, and hence for intervention. Although our previous work suggested a positive association of infant growth with childhood adiposity, assessed from body mass index (BMI), the effects of infant growth on long-term health remain unclear because BMI in early childhood might not track into adulthood, the pubertal growth spurt may exert a modifying influence and BMI may reflect both build and adiposity. Moreover rapid infant growth might have compensatory benefits, such as more robust development of the immune system.

Objectives: Test the hypotheses that rapid infant growth is associated with adverse cardiovascular outcomes, proxied by BMI, waist circumference, waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR) at 13 years, but also with immunological benefits proxied by less hospital use due to infections until 13 years.

Methods: We used multivariable linear regression in respectively 6861 and 5476 participants from a Chinese birth cohort (n=8327), "Children of 1997", comprising 88% of births in Hong Kong in April and May 1997, to examine the adjusted association of infant growth (at 0 to 12 months) with BMI and WHR at 13 years. We also used multivariable negative binomial regression to examine the adjusted association of infant growth with subsequent hospital admissions for infections.

Results: Being born heavy for gestational age and fast infant growth were associated with higher BMI and a greater waist circumference, but not higher WHR at 13 years in both boys and girls. Fast infant growth was only associated with WHtR among boys and it was not associated with fewer hospital admissions for infections at any stage of life.

Conclusions: Fast infant growth was not associated with immunological benefits in Hong Kong children. Varying associations of infant growth with different adiposity measures suggest a complex role of infant growth in long-term health perhaps because infant growth (or its underlying drivers) influences body build and body composition as well as adiposity. How infant growth affects body composition, whether the associations vary by sex and whether associations observed during adolescence persist into adulthood remain to be determined.

Ref. No.: 08090761

P8-Ab0028
To Determine the Prevalence of Osteonecrosis of the Jaw in Patients who take Bisphosphonate for Osteoporosis Treatment

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Introduction: Osteonecrosis of the Jaw (ONJ) is a serious condition which is difficult to treat. Bisphosphonate-Related Osteonecrosis of the Jaw (BRONJ) is a well-known complication in patients receiving high dose intravenous bisphosphonate for the treatment of metastatic bone disease. In recent years, there have been reported cases of BRONJ in post-menopausal women receiving oral bisphosphonate for the treatment of osteoporosis as well.

Aims: Determine the prevalence of osteonecrosis of the jaw in patients on chronic bisphosphonate for osteoporosis treatment.

Methods: Patients with history of 3 years or more of oral bisphosphonate treatment for osteoporosis were invited to the telephone interview using a dental screening questionnaire. The questionnaire was designed by a dental surgeon experienced

in managing BRONJ. For those who reported any suspicious symptoms of BRONJ, we tried to find out the dental records for BRONJ confirmation. If those records were not available or the records did not contain clear information about the diagnosis, the subjects were invited to have a dental examination for the confirmation of ONJ.

Results: One thousand two hundred and eighty-four eligible subjects completed the screening questionnaire by telephone, the response rate being 62.8%. There were four clinically confirmed cases of BRONJ. The prevalence of BRONJ in our study was 0.3% with a frequency of 73.53 per 100,000 person-years of oral bisphosphonate treatment. Three of the patients had tooth extraction and none of them had regular dental visits.

In conclusion, the prevalence of BRONJ in our study was relatively high. Most of them were related to tooth extraction.

Ref. No.: 09100831

P9-Ab0140
A Study on the Pharmacological Interactions between a Chinese Herbal Formula ELP and Standard Anti-resorptive Drugs Used to Counteract Osteoporosis

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Anti-resorptive drugs alendronate and raloxifene are effective in lowering bone mineral density (BMD) loss in post-menopausal women. However, long-term treatment may be associated with serious side effects. Our research group has recently discovered that a Chinese herbal formula ELP could significantly reduce BMD loss in animal and human studies. Therefore, the present study aimed to investigate the potential synergistic bone-protective effects of different herb-drug combinations using ovariectomized rats. To assess the efficacy of different combinations, the total BMD was monitored biweekly in the 8-week course of daily oral treatment. Bone micro-architecture, bone strength and deoxypyridinoline level were also determined after 8 weeks. From our results, co-administration of ELP and raloxifene increased the total tibial BMD by 5.26% (2.5 mg/kg/day of raloxifene; P=0.014) and 5.94% (0.25 mg/kg/day of raloxifene; P=0.026) when compared with the respective dosage groups with raloxifene alone. Similar synergistic effects were also observed in BMD increase at distal femur (0.25 mg/kg/day; P=0.001) and reduction in urinary deoxypyridinoline crosslink excretion (2.5 and 0.25 mg/kg/day; Both P=0.02). However, such interactions could not be observed in all alendronate-treated groups. Using Bioassay-guided fractionation, we found that the icariin-containing F7 sub-fraction possessed the most potent osteoblastic and anti-osteoclastic effects. This fraction could exert synergistic effects with the raloxifene in vitro. Our data provide first evidence that ELP could synergistically enhance the therapeutic effects of raloxifene, so that the clinical dosage of raloxifene could be reduced.

Ref. No.: 08090301

P10-Ab0036
Estimating the Effect of Cold Weather and Cold Spells on Mortality in 3 Asian Cities: Hong Kong, Taipei and Kaohsiung

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Background: Numerous studies have found associations between extreme temperatures and human mortality but relatively few studies have been done in sub-tropical and tropical cities, especially in Asia.

Objectives: To examine the impact of cold temperatures and cold waves on mortality in 3 subtropical and tropical Asian cities.

Study Design: Analysis of daily mortality time-series using Generalized Additive Models with daily mean temperature as the main explanatory variable and humidity, pollutants (nitrogen dioxide (NO_2), sulfur dioxide (SO_2), respirable suspended particulates (RSP), ozone (O_3), seasonality and flu consultation rates (for Hong Kong) controlled as potential confounders.

Setting and Subjects: The settings are the cities of Hong Kong, Taipei and Kaohsiung. The subjects are all natural deaths in Hong Kong, during the cool season between 1999 and 2009 and between 1999 and 2008 for Taipei and Kaohsiung.

Main Outcome Measures: Daily time-series of natural deaths for the 3 cities. Subgroup analysis was also done by gender, age group, cause of death and geographical area of residence.

Results: Cold temperatures were strongly associated with higher mortality with lagged effects persisting up to 3 weeks in Hong Kong and 2 weeks in the Taiwanese cities and cold effects were much stronger for deaths among older people and non-cancer deaths. Prolonged cold spells modestly but significantly raised mortality after accounting for the effects of individual cold days. Higher daily ozone levels were also strongly associated with higher short-term mortality in Taipei and Hong Kong, while other meteorological parameters including relative humidity and solar radiation were weakly and inconsistently associated with mortality.

Limitation: Since this was a population based study and temperature was measured at a single fixed monitoring station we cannot be sure of the extent to which are measurement of exposure corresponds to the actual temperatures to which subjects were exposed.

Conclusions: Cold temperatures and cold spells substantially increase short-term mortality in sub-tropical Asian cities particularly among the elderly.

Implications: Greater attention needs to be paid to the adverse health effects of cold temperatures. Interventions including provisions of shelters, cold weather warnings and education about the possible health effects of cold temperature should be carried out in sub-tropical areas.

Ref. No.: 09100811

P11-Ab0049
Familial Aggregation of Insomnia in Hong Kong Chinese: A Prospective, Case-control Study

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Aims: In this two-phase study, we aimed to 1) explore the longitudinal changes of insomnia in both children and their parents; 2) confirm the familial aggregation and heritability of insomnia by detailed clinical interviews; 3) explore the potential biological markers of insomnia.

Methods: Phase 1 study: The package of brief questionnaires for adolescents, their siblings, fathers and mothers were mailed to

the 3416 families, among which 1611 families (47.1%) returned. Phase 2 study: A total of 236 families were invited into phase 2 study. A case-control study with detailed clinical, sleep, psychiatric and biological assessment were conducted in adolescents with insomnia (n=75) without insomnia (n=161) as well as their first-degree relatives.

Results: Phase 1: The persistence rate of insomnia was 44.6% for mothers, 24.8% for fathers, and 14.9% for adolescents. Insomnia at baseline was significantly associated with poorer mental and physical health in recent one year in both adolescents and adults (p<0.05). Phase 2 study: Heritability analysis showed that the heritability ± SE was 0.48 ± 0.19 for current insomnia and 0.61 ± 0.13 for lifetime insomnia. The phenotypic associations of insomnia symptoms with pain and somatic measures were both contributed by genetic (range p(G)=0.41-0.96) and environmental (range p(E)=0.27-0.40) factors with a major genetic contribution. Adults with insomnia had a significantly greater cortisol awakening response (CAR) reference to increase (CARi) but a comparable CAR reference to ground and a comparable cortisol level during afternoon and evening when compared with non-insomniac adults. The association between insomnia disorder and higher CARi was found in adolescents at late/post puberty but not in pre/early pubertal adolescents. There was an interaction effect between sex and insomnia disorder on CARi level with adult females having higher CARi than adult males.

Conclusions: Insomnia is commonly found in both adolescents and adults with moderate persistence rate and adverse physical and mental consequences at 5 years follow-up in Hong Kong Chinese general population. Insomnia is a highly heritable disorder with robust familial aggregations. Hyperarousal mechanism involves in the pathophysiology of insomnia. Our findings strongly suggested the necessity of early and intensive management as well as further molecular genetic investigation of insomnia.

Ref. No.: 08090011

P12-Ab0056
Is Assertive Community Treatment an Effective Intervention for Frequent Readmissions to Psychiatric Hospital

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Introduction: Modern psychiatric practice is shifting from institutional to community care. Experiences overseas showed undesirable consequences arising from hasty deinstitutionalization overseas. Case management model, which had been widely used in social work, insurance, employment and legal system had been shown effective in community mental health services. We have confirmed earlier in a randomized control study, that case managers in Hong Kong could reduce the admission rate, encouraged higher discharge and lowered the length of stay of chronic severely ill mental patients. In this study, we explored the effectiveness of Assertive Community Treatment (ACT) for severely ill mental patients during a period of rapid deinstitutionalization in Hong Kong.

Methods: A flanking historical control design was employed. The treatment group comprised participants with 3 or more admissions to psychiatric hospitals within the preceding 12 months, and received ACT. Two historical control groups (C_1 and C_2), with similar inclusion criteria flanking the recruitment period of

treatment group, were identified and received Treatment as Usual (TAU). Outcome data were measured at baseline, 6, 12 and 18 months.

Results: 210 participants were recruited, with 70 in each of the ACT, C_1 and C_2 TAU groups. Readmission rates, bed-days, A&E attendances and days of missing medical appointments improved during the deinstitutionalization process, irrespective of treatment modality. In addition, ACT had superior effect in most of these outcome parameters, compared to the TAU groups.

Conclusions: We employed historical control design, using two TAU control groups flanking the recruitment/treatment period of ACT group, in parallel with the deinstitutionalization process. The outcome variables improved with time in all groups, irrespective of treatment models. We confirmed that the current model of ACT, with a relatively small case load per case manager, round the clock services, multidisciplinary team approach, with psychiatrists integrated in the services and case managers responsible for health and social care, is an effective intervention for helping persons with mental illness pursue their chosen independent living in the community. The Recovery-oriented ACT had additional beneficial effect in most of the outcome compared to the TAU groups, on top of the effect from deinstitutionalization.

Ref. No.: SMH-39

P13-Ab0057
Risk of Perioperative Respiratory Complications and Postoperative Morbidity in Adults Exposed to Active and Passive Smoking before Surgery

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Introduction: Tobacco smoking increases the risk of perioperative complications. However, the effect of passive smoking on the risk of perioperative complications in adults is unknown. This study estimated the prevalence of active and passive smoking before surgery and evaluated its effect on the risks of perioperative respiratory complications and postoperative morbidity.

Methods: We conducted a prospective cohort study of 736 adult patients receiving general anaesthesia for major elective surgery. Patients were classified according to their self-reported smoking history and urinary cotinine concentration within 48 hours before surgery. The main outcomes were composite measures of perioperative respiratory complications and postoperative morbidity on the third day after surgery. The urinary cotinine concentration was measured using liquid chromatography-tandem mass spectrometry analysis by research staff blinded to the clinical outcomes. A generalized estimating equation model was used to estimate the common-effect relative risk of the perioperative respiratory complications and postoperative morbidity composite endpoints associated with smoking status.

Results: There were 313 (42.5%) nonsmokers, 92 (12.5%) passive nonsmokers, 157 (21.3%) ex-smokers without environmental tobacco smoke (ETS) exposure, 53 (7.2%) passive ex-smokers and 121 (16.4%) smokers. The overall incidence of perioperative respiratory complications and postoperative morbidity were 9.5% (95% CI, 7.5%-11.8%) and 29.2% (95% CI, 26.0%-32.6%), respectively. The association between smoking status and the risks of perioperative composite endpoints after adjusting for demographic, surgical and preoperative respiratory

comorbidity factors were determined.

Conclusions: One in five adults was exposed to ETS before surgery. Passive cigarette smoking showed very little, if any, increased risk of perioperative respiratory complications. Both active and passive exposure to tobacco smoke increased the risk of postoperative morbidity. Taking a preoperative history that includes both active and passive exposure to tobacco smoke may identify high-risk patients for perioperative-related complications.

Ref. No.: 08090311

P14-Ab0059
Designing Culturally Appropriate Health Education Messages on Alcohol Consumption for Young Adults in Hong Kong

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Introduction: In 2007, the Hong Kong government enacted legislation to reduce the alcohol taxes on beer and wine in the SAR as a stimulus to the food and beverage industry. In combination with the ready accessibility of alcohol, these tax reductions are likely to increase the alcohol consumption rates among young adults. Despite these recent developments, factors associated with alcohol consumption among young drinkers have not been carefully scrutinized in the local context. The captioned study examines young adults drinking with a focus on personal and environmental factors that may affect consumption patterns.

Methods: Six focus groups were conducted in 2013 with 29 Hong Kong Chinese residents between ages 18-25, recruited with the cooperation of young adult-affiliated organizations via flyers, mailing lists, and online forums and games. A modified version of framework analysis was employed to guide the coding and analysis processes, with additional codes generated from repeating concepts from the data unexplored in previous literature.

Results: The study sample perceived alcohol use in a positive light, especially in regards to its benefits in social situations. A high level of physical availability of alcohol was viewed based on the convenience and comfort of bars and lounges for social gatherings and accessibility of beverages at convenience stores. Binge drinking in particular was viewed by young adults as a common practice stemming from a need to maintain "face" in social situations. Females were found to be more susceptible to undesired drinking.

Conclusions: Compared to tobacco and recreational drugs, alcohol use and the context of its consumption, have not been as well researched in Hong Kong. Given their generally positive perception of the social benefits of alcohol use, and the city's permissive drinking environment, Hong Kong's young adults are highly susceptible to alcohol-related harms. Alcohol policy that restricts physical cues and availability of alcoholic beverages should be considered and strictly enforced. Public health and youth service workers should familiarize themselves with the social assertiveness, "face" maintenance and gender repression as possible forces influencing youth alcohol use for designing health promotion campaigns and interventions.

Ref. No.: 10110971

P15-Ab0142
Transplacental Transfer of Melamine

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In 2008, the melamine outbreak alerted people all around the world and raised public concern about food safety. Adulteration of melamine to increase nitrogen content of the dairy products led to severe renal failure and even death of infants. Because melamine causes adverse health effects in infants and young children, neonatal exposure may harm the development of the fetus. This study aimed to investigate the transfer of melamine through human placenta by ex vivo human placental perfusion. Altogether nine out of eighteen human placentas were successfully perfused for 4 hours either with 10μM (n=3) or 1 mM (n=3) melamine alone, or 10 μM melamine in combination with 10 nM cyanuric acid (n=3). Although the transfer of melamine was significantly slower than that of the passively diffusible reference compound antipyrine, it was significantly transferred with, about 41%, 45% and 35% of melamine found in the fetal circulation when either 10 μM or 1 mM of melamine alone, or melamine in the presence of cyanuric acid was used, respectively. Additionally, cytotoxicity of melamine and cyanuric acid was also evaluated in BeWo cells by MTT assay. Neither melamine nor cyanuric acid alone was cytotoxic within the used concentrations. However, cytotoxicity was observed with the combination of 2 mM melamine with 2μM cyanuric acid after a 48-hour exposure. Our results provide the first direct evidence of transfer of melamine through human term placenta. This indicates that the exposure of pregnant mothers to melamine may also lead to neonatal exposure and harmful health effects on fetal development.

Ref. No.: MI-BS-16

P16-Ab0063
Randomized Controlled Trial of the Self-Stigma Reduction Program among Individuals with Schizophrenia

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Individuals with schizophrenia are prone to self-stigmatization, which reduces their psychosocial treatment adherence. A self-stigma reduction program was developed based on a theoretical framework proposed by our team. The effectiveness of such program to reduce self-stigma, enhance readiness for change, and promote adherent behaviors among individuals with schizophrenia was investigated. This program consisted of 12 group and four individual follow-up sessions. An integrative approach including psychoeductaion, cognitive behavioral therapy, motivational interviewing, social skills training, and goal attainment program was adopted. Sixty-six self-stigmatized individuals with schizophrenia were recruited. They were randomly allocated to the self-stigma reduction program (N=34; experimental protocol) or the newspaper reading group (N=32; comparison protocol). Measures on participants' level of self-stigma, readiness for change, insight, general self-efficacy, and treatment adherence were taken for six assessment intervals. The findings suggested that the self-stigma reduction program has potential to reduce self-esteem decrement, promote readiness for changing own problematic behaviors, and enhance psychosocial treatment adherence among the self-stigmatized individuals with schizophrenia during the active interventional stage. However, there was a lack of therapeutic maintenance effects during the 6-month follow-up period. Recommendations for further improving

the effectiveness of self-stigma reduction program are suggested.

Ref. No.: 04060091

P17-Ab0074
Pathological Internet Use and Associated Factors Among University Students in Hong Kong: A Cohort Study

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Introduction: Although Internet use is nearly ubiquitous among university students in Hong Kong, there are only a limited number of local studies examining the potentially harmful health effects of Internet use in this population.

Methods: This prospective cohort study followed 1027 local undergraduates from the commencement of their studies in order to determine the pervasiveness of pathological Internet use (PIU) and the associated factors with self-administered survey.

Results: After 1.5 years of university, the prevalence PIU increased more than three-fold from 5.0% to 15.7%. The study also showed significant associations between PIU and other aspects of health such as inadequate sleep, worsened mental well-being, and worsened family relationships. Students from Mainland China (Adjusted Odds Ratio = 1.89), students who were dissatisfied with university life (AOR = 1.98), and students with higher level of depressive symptoms at baseline (AOR = 1.08 per 1 point increase in CESD-10 score) were particularly noted to be at higher risk for PIU. Most university students with PIU were not cognizant of their pathological Internet use; moreover, only 11.8% of students with PIU expressed strong interest in seeking help for their problematic internet use.

Conclusions: Given these findings, university health services should bear in mind that PIU is a common health issue of students that may link to a multitude of other health concerns. Pro-active efforts will be required by health services to increase awareness and to encourage proper management of PIU among university students.

Ref. No.: 06070471

P18-Ab0081
Can We Predict Postoperative Cardiac Complication with Endotheial Function Test?

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Background: Perioperative myocardial ischemia is a common complication after noncardiac surgery that is associated with serious morbidity and mortality. Endothelial dysfunction may play an important role in perioperative myocardial ischemia and its rapid assessment may provide a novel method of risk stratification prior to surgery.

Methods: We studied patients scheduled to undergo intermediate or high risk surgery in a prospective study to determine whether preoperative endothelial dysfunction identified by a Reactive Hyperemia - Peripheral Arterial Tonometry (RH-PAT) index could provide effective risk stratification for perioperative myocardial ischemia, defined as serum troponin T concentration > 0.03 μg/l within 3 postoperative days.

Results: The primary outcome occurred in 15% of patients. An RH-PAT index ≤1.22 was used to define endothelial dysfunction. Adjusted for age, revised cardiac risk index and a composite measure of the extent of surgery, endothelial dysfunction was strongly associated with perioperative myocardial ischemia (odds ratio 10.6, 95% CI 3.4-33.0, p=0.001) as well as an increased time to discharge from hospital after surgery (hazard ratio 0.39, 95% C.I. 0.24-0.65, p=0.001). Endothelial dysfunction identified myocardial ischemia with sensitivity of 31%, specificity of 96% and a positive diagnostic likelihood ratio of 8.0. Risk classification for myocardial ischemia was improved by the addition of RH-PAT defined endothelial dysfunction to the revised cardiac index (c-statistic increased from 0.72 to 0.80; integrated discrimination improvement 0.11, p=0.004).

Conclusions: For patients undergoing noncardiac surgery, the non-invasive assessment of endothelial function may offer effective preoperative risk stratification, both alone and synergistically when combined with a readily available existing clinical risk score, for perioperative myocardial ischemia.

Ref. No.: 07080421

P19-Ab0087
The Neuroeconomics of Willingness-to-pay in Healthcare Finance

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Introduction: A study of willingness-to-pay(WTP) helps us understand the mechanism of economic exchange. Its asymmetric preference over a range of financial choices has been underpinned by Kahneman et al. We would like to investigate WTP in the setting of healthcare financing options i.e."loss" domain. We explored the neural substrate of decisions to test the hypothesis that differential activation of brain centres affiliated with emotion may occur with the comparison of low-versus-high actuarially-fair values but not with the comparison of low-versus-high probability of illness.

Methods: We designed four packages with the following actuarially-fair values: Rare but important illness(1/500 of paying $5000=$10), treatable common illness(1/60 of paying $6000=$100), disaster plan(1/600 of paying $120,000=$200) and categorical chronic illness(1/50 of paying $150,000=$3000). The participants were asked how much to pay from year to year based on the precinct that subsidies from the Government may change. They may buy any or all of the packages. A subgroup of participants underwent a simplified version of the questionnaire as part of the neuroeconomic study inside a functional magnetic resonance imaging(fMRI) scanner using the method of finding the certainty equivalent by Paulus et al. The fMRI paradigm was written in E-prime and the echoplanar images were analyzed with statistical parametric mapping(SPM5).

Results: 208 participants with a mean age of 33.9 years and 55.5% male gave an overall acceptability of 81.8% for all the packages. The most popular package was disaster plan (87.3%) and the least popular package was categorical chronic illness (77.9%). The WTPs for the packages were $43.4,$145.4,$295,$2580 respectively. The most prominent

degree of overweighing for packages 1-3 and underweighing of package 4 occurs with the age group 50-59 years ($34.9,$142.2, $374.2,$2133). The least degree of overweighing packages 1-3 and underweighing package 4 occurs with the age group 60+ years ($48.5, $179.1,$247.5,$3080). The amount of WTP was proportional to income with the highest WTPs observed with monthly income>$50,000 ($47.2,$176.6,$392,$3002). For the fMRI study 21 participants produced BOLD signals in brain areas for packages 1-4(bilateral temporal regions, posterior temporal regions, right temporal region and bilateral frontal regions). A t-test with contrast 1/0 between packages with low versus high actuarially-fair values produced differential activation in right inferior frontal region. The test comparing low-versus-high probability of illness produced no significant differenital activation.

Conclusions: Asymmetrical preference of WTP was demonstrated with healthcare financing options with probable activation of emotional brain centres while evaluating high versus low actuarially-fair insurance packages.

Ref. No.: 06070461

P20-Ab0094

High-Dose Simvastatin for Aneurysmal Subarachnoid Haemorrhage (HDS-SAH): A Multi-centre Randomised Controlled Double-blinded Clinical Trial

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Background and Aims: Experimental evidence has indicated the benefits of simvastatin for the treatment of subarachnoid haemorrhage. Two randomised, placebo-controlled pilot trials that used the highest clinically approved dose of simvastatin (80 mg daily) gave positive results despite a lower dose of simvastatin (40mg daily) did not improve clinical outcomes. We hypothesised that a high dose of 80 mg of simvastatin daily for 3 weeks would reduce the incidence of delayed ischaemic deficits following subarachnoid haemorrhage compared with a lower dose (40 mg of simvastatin daily) and lead to improved clinical outcomes.

Methods: The study design was a randomised controlled double-blinded clinical trial (ClinicalTrials.gov Identifier: NCT01077206). Aneurysmal subarachnoid haemorrhage patients (presenting within 96 h of the ictus) from six neurosurgical centres were recruited over 3 years. The primary outcome measure was the presence of delayed ischaemic deficits (DIDs), and secondary outcome measures included a modified Rankin disability score (mRS) at 3 months and an analysis of cost-effectiveness.

Results: No difference was observed between the groups treated with the high dose or the lower dose of simvastatin in the incidence of DID (27% versus 24%; odds ratio, 1.2; 95% confidence interval, 0.7–2.0; p = 0.586) or in the rate of favourable outcomes (mRS 0–2) at 3 months (73% versus 72%; odds ratio, 1.1; 95% confidence interval, 0.6–1.9; p=0.770).

Conclusions: High-dose simvastatin treatment should not be prescribed routinely for aneurysmal subarachnoid haemorrhage. Clinical Trial Registration-URL: ClinicalTrials.gov. Unique Identifier: NCT01077206.

Ref. No.: 07080401

P21-Ab0096

8000 Hourly Air Change Rates in a Naturally Ventilated Hospital in Hong Kong

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Introduction: WHO (2009) published a guideline on use of natural ventilation for infection in hospitals. However, there is no long term performance data, which is urgently needed as the seasonal change of natural driving forces and human behavior in window opening can be very significant. This project is to measure yearly ventilation rates in the Grantham Hospital (GH), and to study the factors that affect performance of natural ventilation. For comparison, we also measured the mechanical ventilation rate in 6 TB isolation rooms at Wong Tai Sin Hospital (WTSH).

Methods: The measurement was conducted continuously from July 2009 to January 2011. Ventilation rates were mainly measured by the carbon dioxide method. A tracer gas method was only used during the renovation period (September-October 2009). We also measured temperature and humidity within and outside of the building, and the airborne bacteria and TB sampling.

Results: We obtained more than 8000 hourly air change rates. The measured hourly air change rates all satisfy the WHO requirement in all 4 cubicles, except some hours in August 2010 in one of the cubicles. In general, the air change rates in the WTSH wards rooms satisfied the minimum ACH requirement of 12 ACH, but not as well ventilated as GH.

Grantham Hospital recorded the lowest indoor bacteria count, only 14% increase relative to its roof value for the 24 hour incubation data and 7% for the 48 hour incubation data. Correspondingly, there is a 179% and 75% increase at WTSH and 602% and 617% increase at SYP. Both SYP and WTSH are mechanically ventilated.

Most of the ventilation rates are achieved by wind ventilation, but also by exhaust fans during low wind periods. Such conclusion confirms the epidemiological data (Seto, unpublished) that the TB rates of the health care workers in the Grantham Hospital are about the same as in other mechanical ventilation TB hospitals. We also learned how the issues of typhoon, no-wind, hot summer are resolved by using balcony design, exhaust fans and spot cooling at Grantham Hospital.

Conclusions: Our study provides strong evidence for the use of natural ventilation in hospitals for infection control as recommended by WHO (2009). Our study also showed that the infiltration of outdoor bacteria into the wards is not an issue as the indoor space is well ventilated. The condensation and mold are the remaining issues to be resolved for use of natural ventilation in hot and humid climate.

Ref. No.: HA-NS-006

P22-Ab0097
How Shared Anteroom Affect Ventilation Performance in a Ward Setting

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Introduction: Ventilation is the commonly-used engineering measure for infection control in negative pressure isolation rooms. One of the design issues is that door opening may play a role when there is a shared anteroom between two isolation rooms. Here is the hypothesis. When one opens a door to an isolation room, the flow vortex induced by door sweeping may lead to air leakage from the isolation cubicle to the anteroom. Before the contaminated air is fully exhausted from the anteroom, the anteroom contaminated air may be further leaked into the newly opened room.

Methods: A series of field measurements were first conducted in the Caritas Medical Centre (CMC) Hospital in 2010. Two tested isolation cubicles (Room 1 with a source manikin and Room 2) with a shared anteroom were located in Ward 8B. The tracer gas SF6 was continuously released from the mouth of the source manikin in Room 1. The tracer gas concentration was continuously monitored at three sampling points in Room 1, 2 and the anteroom respectively. Fifteen experiments were performed. CFD simulations were carried out with realistic door opening and closing to obtain more detailed information with a user defined function (UDF) for realizing the sweeping motion of doors.

Results: As the door remains fully open, the release of smoke parcel reveals a bi-directional airflow through the doorway. We also showed the exchange flow by smoke visualization. The higher temperature in the isolation cubicles than in the anteroom was found to be the driver of such two-way airflows. Both measured data and computer simulations demonstrate a possibility for pollutant spread between two isolation cubicles through the shared anteroom. Up to 19 times and 1.5 times concentration of tracer gas was detected in the anteroom and the neighbouring 'clean' room respectively relative to the background concentration levels.

Conclusions: If the dirty cubicle door is fully open for a while, a significant amount of droplet nuclei can be leaked out of an isolation cubicle into another through the shared anteroom. To reduce the risk of infectious disease spread, the duration of full door opening should be shortened as much as possible. The sweeping motion of door opening and closing is a less important mechanism for droplet nuclei leakage as the process is short, but the temperature difference driven flow is found to be important.

Ref. No.: HA-NS-007

P23-Ab0099
Zinc finger E-box binding factor 1 Plays a Central Role in Regulating Epstein-Barr Virus Latent-lytic Switch and Acts as a Therapeutic Target in EBV-associated Gastric Cancer

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Background: The role of Epstein-Barr virus (EBV) infection in gastric carcinogenesis is still largely unknown. We studied the effect of *zinc finger E-box binding factor 1 (ZEB1)* on latent-lytic switch of EBV infection in gastric cancer, and explored the importance of EBV in gastric carcinogenesis.

Methods: Loss or gain of *ZEB1* function was obtained by *ZEB1* siRNA knock-down or forced *ZEB1* re-expression. Cell growth was evaluated by cell viability and colony formation assays, and cell cycle by Flow Cytometry. EBV was detected using quantitative PCR and *in situ* hybridization.

Results: *ZEB1* knock-down in latent EBV infected gastric cancer cell line YCC10 increased lytic gene *BZLF1* expression and decreased of latent gene nuclear antigen 1 (*EBNA1*) expression, concomitant with the inhibition of cell viability (P < 0.05) and S phase DNA synthesis (P < 0.01). *ZEB1* depletion combined with ganciclovir revealed a further reduction on cell viability (P < 0.001). *ZEB1* knock-down induced cell apoptosis, and upregulation of cleavage of caspase-3 and poly *ADP-ribose* polymerase. On the other hand, ectopic overexpression of *ZEB1* in lytic EBV infected gastric cancer cell line AGS-EBV inhibited *BZLF1* promoter (Zp) activity, *BZLF1* expression and apoptosis, promoted cell growth. EBV infection was detected in 11.3% (80/711) of gastric cancers. EBV existence was associated with age, male gender and intestinal type cancer.

Conclusions: *ZEB1* is a key mediator of the latent-lytic switch of EBV-associated gastric cancer, a distinct subtype with different clinicopathologic features. Inhibition of *ZEB1* may be a potential target for EBV-associated gastric cancer therapy.

Ref. No.: 08070522

P24-Ab0107
The Epidemiology and Natural History of Depressive Disorders in Hong Kong's Primary Care

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Objectives: To estimate and examine the factors associated with prevalence, 12-month incidence and remission rates of depressive disorders in primary care; to examine health service utilization patterns of primary care patients with depression.

Methods: Cross-sectional followed by 12-month cohort observational study.

10,179 (response rate 81.0%) adult patients were recruited from the waiting rooms of 59 primary care physicians (PCPs) to complete a questionnaire which screened for depression. PCPs blinded to screening scores provided information on diagnosis and management. 4,358 (response rate 42.8%) patients were telephoned at 3, 6 and 12 months to monitor symptomatology, health-related quality of life and service use.

Study Instruments: Patient Health Questionnaire-9 item (PHQ-9); Centre for Epidemiologic Studies Depression Scale (CES-D 20); Short-Form Health Survey Version 2.0 (SF-12v2.0)

Results: Cross-sectional prevalence of PHQ-9 positive (PHQ+ve) depression was 10.69%, 12-month incidence was 5.25% and 12-month remission rate was 60.31%. 23.1% of PHQ+ve subjects were diagnosed with depression by the PCP.

Patients at greatest risk for screening PHQ+ve: had a past history of depression; were unemployed; had seen a GP more than twice in the previous month; or had ≥2 co-morbidities.

PCPs were most likely to diagnose depression in: patients with a past history of mental illness; or non-Chinese.

In PHQ+ve subjects, over 12 months, mean SF-12v2 scores returned to normal with 30% improvement in the mental component score and 10% improvement in the physical component score. PCP detection had no effect on remission from depression but detected patients had greater improvements in mental health-related quality of life.

In patients diagnosed with depression by the PCP, 50% were prescribed psychotropic medications and 10% referred to other services, most commonly counsellors. Private-sector PCPs had a 6.75-fold higher likelihood of prescribing medication.

Amongst the cohort sample who screened PHQ+ve at baseline, over 12-months 21.7% had consulted a psychiatrist and 37.5% had taken psychotropic medications.

Conclusions: Approximately one in ten patients presenting to a PCP are symptomatic of depression; over a year, only one in four of these will receive mental healthcare services, with more using a psychiatrist than a PCP. Prescribing rates for depression are high, particularly in the private sector. To help reduce the specialist burden, health policy needs to focus on promoting better recognition and utilization of primary care providers in depression care. Better access to psycho-social services may help reduce prescribing rates. Enhancement of detection rates is needed to enable more patients to receive the appropriate care.

Ref. No.: SMH-27

P25-Ab0114

Reactivation of Growth/Differentiation Factor 1 Contributes to the Chemopreventive Effect of 5-aza-2'deoxycytidine in Gastric Cancer

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Introduction: Helicobacter pylori (HP) is a type 1 carcinogen for gastric cancer (GC), the second most common cause of cancer-related death worldwide. The limited benefit of HP eradication or nutritional intervention in risk reduction and the dismal prognosis of GC underlie the urgent need for new preventive strategies. We have recently shown that Hp causes aberrant DNA methylation of tumor suppressor genes to promote gastric carcinogenesis (ref 1). However, the functional and mechanistic relationships between aberrant DNA methylation and GC remain elusive.

Aims and Methods: We investigated the effect of 5-aza-2'-deoxycytidine (5'Aza-dC), a FDA-approved demethylating agent in a murine GC model induced by N-Nitroso-N-methylurea (MNU). Using MethylCap-microarray, quantitative RT-PCR and Western blot, we identified novel DNA methylation-controlled genes in paired GC tumors/adjacent tissues (4), 5'Aza-dC-treated (3) and -untreated (3) normal mucosa samples, followed by pyrosequencing and gene expression validation in human GC samples and cell lines. Gene functions were investigated by cell cycle and colony formation assays.

Results: At 52 weeks-post MNU exposure, GC was developed in 8 out of 19 mice. Administration of 5'Aza-dC for 24 weeks significantly reduced GC incidence from 42.1 to 11.1% (2/18 mice; p<0.05). Microarray analysis uncovered 12 significant and recurrent hypermethylated genes exclusive in GCs. However, only growth/differentiation factor 1 (Gdf1), a ligand for transforming growth factor-beta (TGF-β) signaling, had significantly lower mRNA expression in tumors compared to both tumor-adjacent and normal tissues (p<0.05). Notably, 5'Aza-dC treatment reactivated Gdf1 expression to the normal mucosal level. In human GCs, aberrant GDF1 methylation (>1.5-fold increase compared to tumor-adjacent tissues) was observed in 58.3% (14 out of 24) cases, which was accompanied with significant GDF1 down-regulation in both mRNA (p<0.005) and protein levels. Compared with normal mucosa, 7/8 GC cell lines exhibited GDF1 silencing, which could be reactivated by genome demethylation. Ectopic GDF1 expression increased SMAD2/3 phosphorylation and significantly suppressed GC cell proliferation at least partially through G1 phase cell cycle arrest.

Conclusions: Our findings demonstrate a causal relationship between DNA methylation and GC development. Epigenetic silencing of GDF1 may abrogate the growth-inhibitory effects of TGF-β signaling and render selective growth advantage to gastric epithelial cells during carcinogenesis. This study lends support to demethylating drugs for GC chemoprevention trial.

Ref. No.: 08070172

P26-Ab0118

A Simulation Study for a Method to Determine Life Expectancy Change due to Air Pollution from Time Series Data

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Background: We have shown that life expectancy (LE) change attributable to air pollution can be determined from coefficients of daily time series (TS) regression model which has a sufficient number of lag days for the exposure variables. However, the validity of the method has not been sufficiently assessed.

Objectives: To assess the robustness of the method, we develop simulated data sets to test the effect of confounders by

M_1: Relative bias = $100 \times (LE_{SO2} - LES_{O2/SO2+ confounder})/LE_{SO2}$

where LE_{SO2} is the true LE change attributable to SO_2 and $LE_{SO2/SO2+\ confounder}$ is the LE change attributable to SO_2 in the presence of confounders. The effects with one and with two pollutants in the presence of correlations between pollutant concentrations are evaluated by

M_2: Variance inflation factor (VIF)

M_3: Relative efficiency = $SE_{LE:SO2}$ /$SE_{LE:SO2/SO2+confounder}$

where SE is the standard error of LE.

Methods: Daily death counts and pollutant concentrations from Hong Kong during the period 1995-2009 are used to simulate data sets for the analysis. After creating simulation data sets for each of the pollutants and combination of pollutants, we added random noises to the relative risk (RR) values and introduced confounders by adding noisy periods. We use the method that involves formulation of the relative risk ΔRR in the following relationship

$$\Delta RR(j) = {}_{(i=0)}\sum_{(imax)} f(i)c(j-i) \qquad (1)$$

We define ΔRR(j) = D(j)/D_{ref}(j) - 1, where D(j) is the observed daily standardized death rate and the reference death rate Dref(j) on day j. The f(i) are impact coefficients that can be estimated from the linear regression model with known exposure sequence of average concentrations {c(j-i)}

from i_{max} (i.e. the maximum lag days) past up to day j in the form of Equation (1).

Results: The relative bias is not large, typically between one and ten percent. The correlations between pollutants introduce large biases for the determination of LE. The VIF are large, indicating problems with multi-collinearity.

Conclusions: Our approach is reasonably robust in the presence of confounding and correlations between pollutants introduce large biases for the determination of LE.

Ref. No.: 08090971

P27-Ab0120
REM Sleep Behavioral Disorder and Psychiatry: A Hidden but Potential Serious Condition. A Case-control Study

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Objectives: To identify the specific clinical and polysomnographic characteristics associated with the REM sleep behaviour disorder (RBD) in psychiatric populations and to look for any early neurocognitive markers.

Methods: This is a case-control study of 40 subjects of RBD with 2 control arms. 1) Healthy control (HC)- Sex- age-matched control subjects recruited from the community; 2) Psychiatric control (PC)- Sex- age-, and diagnoses-matched subjects recruited from psychiatric clinic. All subjects underwent psychiatric, sleep, overnight polysomnography and neurocognitive assessments.

Results: RBD patients reported high prevalence of sleep-related injuries as a result of the dream enacting behaviour. They had more nightmares, depressive and anxiety symptoms than the controls. They also showed more severe degree of loss of REM-related muscle atonia during polysomnographic assessment,

which is regarded as a hallmark of RBD diagnosis. A dosing relationship was observed in olfactory function, suggesting that psychiatric RBD had more olfactory dysfunction.

Conclusions: RBD in psychiatric populations carries significant adverse consequences of sleep-related injuries to self and bed-partners. Its etiology is not simply a psychotropic-induced condition. Instead, a constellation of clinical factors, including nightmares, anxiety and depressive symptoms contributed to the development of RBD in psychiatric patients. The study also suggested there could be early neurodegenerative components but replicated study of larger sample size is warranted. Moreover, longitudinal follow up of the psychiatric RBD cohort for any future development of neurodegeneration is needed.

Ref. No.: 07080011

P28-Ab0121
Melamine and Its Effects on Urine Crystallization Kinetics and Cell Responses

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Introduction, Aims and Objectives: Acute renal failure in cats and dogs were found to be associated with adulterated pet food in early 2007 and by September 2008, there were reports of children in China being admitted with renal stones and/or failure. In both cases, melamine and its co-contaminant cyanurate was responsible for the renal lithaisis event. Our aims are: (1) to investigate the physicochemical behavior of melamine in the renal environment in-vitro and (2) to understand how melamine affects renal cells in cell culture for its damage, oxidative stress, inflammatory response and gene expression.

Methods: A Mixed Suspension Mixed Product Removal (MSMPR) artificial crystallizers (test and control) was the in vitro set-up for crystallization studies of melamine in human urine. A transwell cell culture model was established using standard protocol to investigate effects of melamine on renal cells.

Results: Melamine crystallized out from human urine under acidic conditions (pH4.5 – 5.5). Presence of melamine significantly caused the precipitation of other lithogenic salts - uric acid, calcium oxalate and phosphate. Clinical relevant drugs such as citrate and bicarbonate did significantly reduce melamine crystallization. Cell culture studies revealed that the renal cells undergo oxidative stress and cell damage (LDH release) through physical damage. Cytokine release and gene expression did show inflammatory response.

Conclusions: Melamine crystallizes in acidic urine and can precipitate out other lithogenic salts. Citrate and bicarbonate therapy are effective and cell culture studies suggests that melamine causes physical damage to cells and humoral type of immune response.

Ref. No.: MI-BS-07

P29-Ab0127

Evaluation of a Model of Violence Risk Assessment (HCR-20) among Adult Patients Discharged from a Gazetted Psychiatric Hospital in Hong Kong

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Background: The community has become increasingly interested in violent risk assessment and strategies in Hong Kong after several homicides were alleged committed by mentally ill patients in recent years. An unstructured clinical model of violence risk assessment, the Priority Follow-up (PFU) system is employed in Hong Kong. However, internationally, structured professional judgement (SPJ) method has been considered as a more useful approach. The Historical/Clinical/Risk Management – 20 items (HCR-20) is the SPJ instrument that most research has been published on. This has not been validated previously in a predominately Chinese population.

Objectives: To test the interrater reliability and predictive validity of the HCR-20, and also compare the predictive validity between HCR-20 and PFU system.

Methods: This was a prospective cohort study.

Setting and Subjects: HCR-20 assessment was completed by trained raters for 110 discharged patients with a PFU status from general adult or forensic psychiatric teams in Castle Peak Hospital and also for the same number of demographically-matched controls.

Main Outcome Measures: Violence, as defined by the HCR-20 manual, was determined from case notes at 6- and 12-month after the HCR-20 rating.

Results: HCR-20 could be rated with acceptable interrater reliability. The predictive validity of the structured final risk judgement was significant, yielding moderate to large effect sizes, for majority of violent outcomes at six months. It also had significantly better predictive ability for violence against property when compared with the PFU system.

Conclusions: The findings support that the HCR-20 can be used reliably for assessment of post-discharge violence in both general adult and forensic psychiatric patients in Hong Kong.

Implications: HCR-20, an evidence-based risk assessment tool, should be considered for introduction into Hong Kong to improve the current practice of violent risk assessment and management.

Ref. No.: SMH-45

P30-Ab0025

Understanding Health-Promoting Behaviors and Physical Health of Older Adults with Mental Illness Using the Health Belief Model

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Background: High morbidity of physical illnesses and premature mortality are often observed among older adults with mental illness. Nevertheless, their physical health care is often neglected. Identifying factors affecting the adherence of health-promoting behaviors are important to prevent their early mortality. In view of this, the present study applied the health belief model on the relationship between their health-promoting behaviors and body mass index. Specifically, it was hypothesized that health-promoting behaviors on healthy diet would mediate the relationship between health beliefs in food intake and body mass index.

Methods: A stratified sample of 587 individuals was recruited from various community mental health services in Hong Kong. A total of 237 people with mental illness (55.3% female, mean age = 56.10, SD = 4.94) who were aged 50 or above were included in the analysis. Their health beliefs in healthy diet (i.e., perceived severity, perceived susceptibility, expected benefits, and expected barriers of healthy diet) and health-promoting behaviors related to food intake were assessed using self-report questionnaires. In addition, their body mass index was also obtained through measuring their heights and weights.

Results: It was found that the majority of the participants had an obese (50.2%) or overweight (19.8%) body mass index, which is a risk factor for various chronic health problems. Furthermore, results revealed that among the five factors in the health belief model, perceived barriers (Baxb=.10, SEaxb=.09, CI: .003 to .24) and cues to action (Baxb=-.16, SEaxb=.10, CI: -.37 to -.01) in adopting a balanced diet had significant indirect effects on body mass index through health promoting behaviors related to healthy diet.

Conclusions: Findings highlighted the need to promote healthy diet among older adults with mental illness through increasing their cues to action (e.g., prompts by doctors, caretakers) and reducing their perceived barriers (e.g., availability of nutritious food choices) in adopting a healthy diet. Results may also help health care professionals in designing health care programs that incorporate these elements to promote healthy diet and overall physical health.

Ref. No.: 07080161

P31-Ab0021

Neurocognitive and Psychosocial Outcomes of Obstructive Sleep Apnea in Hong Kong Chinese

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Introduction: Theory-driven studies investigating the consequences of obstructive sleep apnea (OSA) on neurocognitive and psychological functioning in Chinese populations were lacking. This study aimed to systematically investigate the neuropsychological functioning of Hong Kong Chinese with OSA.

Methods: Twenty-five patients with moderate to severe OSA and 30 healthy controls were recruited from the Sleep Disorders Centre of Queen Mary Hospital and the community, respectively. Participants were assessed on a comprehensive neuropsychological battery including tests of general cognitive functioning, attention and working memory, verbal and visual memory, motor speed and dexterity, and executive functions. Self-reported questionnaires were used to measure sleep quality, daytime sleepiness, mood, quality of life, and functional outcomes.

Results: OSA patients were found to have significantly worse performance on tests of attention lapses, working memory, verbal learning and recall, semantic fluency, and processing speed, with higher sleepiness, poorer sleep quality, more mood symptoms,

and worse functional outcomes and quality of life.

Conclusions: While our findings underscore the universality of cognitive and psychological difficulties encountered by patients with OSA across cultures, the identified profile in our sample of Chinese OSA patients was also distinct from that reported in western populations, with less pervasive deficits in working memory and executive function but impairment in immediate verbal recall in Chinese. These findings serve to provide preliminary data on the neuropsychological profile of Chinese OSA patients. The neurocognitive deficits, mood symptoms, and functional problems identified in this study can also be used as valid outcome measures of treatment efficacy studies.

Ref. No.: 07080971

P32-Ab0035
Effect of Hong Kong's Ban on Smoking in Public Places on Incidence of Acute Myocardial Infarction

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Background: Several studies from Europe and the United States have reported sharp drops in the incidence of acute myocardial infarction (AMI) following the introduction of smoking bans for public places in various cities. In addition some studies have reported that daily AMI hospitalization rates are associated with meteorological conditions, particularly temperature. Hong Kong banned smoking in restaurants, workplaces and outdoor public areas in 2007 and in bars and karaokes in mid-2009. In this study we examine whether AMI hospitalization rates dropped following introduction of the public smoking bans in Hong Kong and also whether daily AMI hospitalizations are influenced by meteorological conditions.

Methods: Data on all public hospital AMI admissions from Hong Kong were collected from 2000-2009 were collected. Generalized additive Poisson regression models were used to model the association between time trend, seasonality and meteorological variables and daily AMI admissions.

Results: The mean number of daily AMI admissions was 13.6. Before the introduction of the first smoking ban there was no consistent long-term trend in AMI hospitalization which first rose from 2001-2003, then declined until 2006. Hospitalizations rose slightly in 2007 and then sharply beginning in late 2008. Neither phase of the smoking ban was accompanied by a notable drop in hospitalizations. In terms of seasonality hospitalizations peaked December-February and were lowest from May-October. Colder temperatures were associated with more AMI hospitalization with an approximate 4% increase in hospitalization being associated with a 1C lower mean temperature over the previous 21 days. Higher humidity was modestly associated with fewer hospitalizations.

Discussion: Unlike previous studies our study did not find a sharp drop in AMI hospitalizations following the introduction of a public smoking ban. Other factors may influence long-term trends in AMI. Further observation of the AMI hospitalization rates in the future is necessary.

Ref. No.: 08090611

P33-Ab0062
Prevalence and Characteristics of Hardcore Smokers in Hong Kong: Before and After the Smoking-free Legislation in 2007

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Introduction: With increasing effort being directed towards tobacco control measures including tobacco tax increase, bans on advertisements of tobacco products on broadcast and printed media in 1980 and the implementation of the smoking-free legislation in 2007, the overall smoking prevalence in Hong Kong declined gradually from 15.7% in 1990, to 11.8% in 2008. However, in 2008, there were still 679,500 daily smokers aged ≥15 years old, and 55.5% of whom had never tried and did not want to give up smoking.

Objectives: To describe the prevalence of hardcore smoking, identify its correlates and compare the awareness of existing smoking cessation services in Hong Kong.

Methods: Repeated cross-sectional surveys of the general population in Hong Kong. We used data from all the daily smokers in Thematic Household Surveys carried out in 2005 (N=3,740) and 2008 (N=2,958). Logistic regression models identified the factors associated with hardcore smoking.

Results: The proportion of hardcore smokers among current Hong Kong daily smokers increased from 21.8% in 2005 to 27.4% in 2008. Compared with their non-hardcore counterparts, they were more likely to be older, male, unmarried and to have started smoking under the age of 20; they were more likely to continue smoking because of both internal and external psychosocial factors. There were changes in the magnitude of some of the predictors of hardcore smoking in both the overall sample and the male sub-sample between 2005 and 2008. Hardcore smokers were less likely to report being aware of existing cessation services. The results for the female sub-group, however, were not reliable because of small sample size.

Conclusions: There appeared to be a hardening of the smoking population in Hong Kong, with a particular demographic profile for hardcore smokers being found. This observed hardening might be driven by psychosocial factors, some of which seem to have altered their impact on hardcore smoking since the implementation of smoke-free legislation. The level of awareness of existing smoking cessation services was lower among hardcore smokers than among ordinary smokers.

Implications: More public information campaigns should be implemented to raise public awareness of existing cessation services among all smokers and motivate them to quit, and more community-based tobacco control programmes should be introduced to help all smokers to give up. Additionally, more effective and tailored cessation treatment, focusing on self-efficacy in resisting smoking, is clearly needed to help hardcore smokers in Hong Kong.

Ref. No.: 08090911

P34-Ab0022
10-year Outcome Study of an Early Intervention Program for Psychosis Compared with Standard Care Service in Hong Kong

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Introduction: Despite evidence on the short-term benefits of early intervention (EI) service for psychosis, long-term outcome studies are limited with inconsistent results. Current study examined the 10-year outcomes of patients with first-episode psychosis who received two-year territory-wide EI service compared with those who received standard care (SC) in Hong Kong using an historical control design.

Methods: Consecutive patients who received the EI service between 1st July 2001 and 30th June 2002, and with diagnosis of Schizophrenia-spectrum disorders, were identified and matched with patients who received SC first presented to the public psychiatric service from 1st July 2000 and 30th June 2001. 148 matched pairs of patients were identified. Cross-sectional information on symptomatology and functioning was obtained through semi-structured interview; longitudinal information on hospitalization, functioning, suicide attempts, mortality and relapse over 10 years was obtained from clinical database. 70.3% (N=104) of SC and 74.3% (N=110) of EI patients were interviewed.

Results: Results suggested that EI patients had reduced suicide rate ($\chi^2_{(1)}$=4.35, p=0.037), fewer number (OR=1.56, $\chi2$=15.64, p<0.0001) and shorter duration of hospitalizations (OR=1.29, $\chi2$=4.06, p=0.04), longer employment periods (OR=-0.28, $\chi2$=14.64, p<0.0001) and less suicide attempts ($\chi2$=11.47, df=1, p=0.001) over 10 years. At 10-years, no difference was found in psychotic symptoms, symptomatic remission and functional recovery.

Conclusions: The short-term benefits of EI service on number of hospitalizations and employment sustained after service termination, but the differences narrowed down. This suggested the need of evaluating the optimal duration of EI service.

Ref. No.: SMH-28

P62-Ab0135
Sputum Microbiota in Tuberculosis as Revealed by 16SrRNA Pyrosequencing

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Background: Tuberculosis (TB) remains a global threat in the 21st century. Traditional studies of the disease are focused on the single pathogen Mycobacterium tuberculosis. Recent studies have revealed associations of some diseases with an imbalance in the microbial community. Characterization of the TB microbiota could allow a better understanding of the disease.

Methods and Results: Here, the sputum microbiota in TB infection was examined by using 16S rRNA pyrosequencing. A total of 829,873 high-quality sequencing reads were generated from 22 TB and 14 control sputum samples. Firmicutes, Proteobacteria, Bacteroidetes, Actinobacteria, and Fusobacteria were the five major bacterial phyla recovered, which together composed over 98% of the microbial community. Proteobacteria and Bacteroidetes were more represented in the TB samples and Firmicutes was more predominant in the controls. Sixteen major bacterial genera were recovered. Streptococcus, Neisseria and Prevotella were the most predominant genera, which were dominated by several operational taxonomic units grouped at a 97% similarity level. Actinomyces, Fusobacterium, Leptotrichia, Prevotella, Streptococcus, and Veillonella were found in all TB samples, possibly representing the core genera in TB sputum microbiota. The less represented genera Mogibacterium, Moryella and Oribacterium were enriched statistically in the TB samples, while a genus belonging to the unclassified Lactobacillales was enriched in the controls. The diversity of microbiota was similar in the TB and control samples.

Conclusions: The composition and diversity of sputum microbiota in TB infection was characterized for the first time by using high-throughput pyrosequencing. It lays the framework for examination of potential roles played by the diverse microbiota in TB pathogenesis and progression, and could ultimately facilitate advances in TB treatment.

Ref. No.: 09080442

P63-Ab0007
Attitudes, Beliefs and Knowledge Concerning Antibiotic Use and Resistance of the General Public in Hong Kong: A Combined Qualitative and Quantitative Study

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Background: The overuse of antibiotics is one of the main causes of the global antibiotic resistance. In Hong Kong, antibiotics are often prescribed for upper respiratory tract infections though little is known about the local public's knowledge, attitudes and behaviour in antibiotics.

Objectives: This study examined these aspects from the local adults aged 18 or above for future strategy to prevent antibiotic resistance.

Methods: The study adopted a combined qualitative and quantitative approach. Eight focus groups and four in-depth individual interviews on participants of different socio-economic levels were conducted at social-service centres. The qualitative data collected were used to construct a questionnaire for the territory-wide telephone survey which recruited 2471 valid responses (response rate of 68.3%) randomly.

Results: Focus-group participants were unclear about the nature and causes of antibiotic resistance; 9.0% of the survey respondents even had not heard of the term. Among the survey respondents, 66.6 % and 64.8% agreed that the purchase of antibiotics without prescription and incomplete courses of antibiotics would lead to undesirable consequences respectively. Only 62.5% had always finished the full course of antibiotics, 7.7% acquired non-prescription antibiotics, and 6.1% kept the leftover. There was no statistically significant association between these attitudes and practices. The focus group participants attributed abuse to the doctors' responsibility, 46.7% of the survey respondents disagreed that they could help the prevention of resistance.

Conclusions: Our study showed that the public was not aware of their role and capability in preventing antibiotic resistance. A large proportion of the public needs education on the use of antibiotics and the medical professionals have a very significant role to play.

Ref. No.: 09080852

P64-Ab0008
The SARS-Coronavirus Membrane Protein Induces Apoptosis via Interfering PDK1-PKB/Akt Signaling

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A number of viral gene products are capable of inducing apoptosis through interfering with various cellular signaling cascades. We previously reported the pro-apoptotic property of the SARS-CoV Membrane (M) protein and a downregulation of the phosphorylation level of the cell survival protein kinase B (PKB/Akt) in cells expressing M-protein. We also showed that over-expression of 3-phosphoinositide-dependent protein kinase-1 (PDK1), the immediate upstream kinase of PKB/Akt, suppressed M-induced apoptosis. This illustrates that M-protein perturbs the PDK1 and PKB/Akt cell survival signaling pathway. In this study, we report that the C-terminus of M-protein interacts with the Pleckstrin Homology (PH) domain of PDK1. This interaction disrupted the association between PDK1 and PKB/Akt, and led to downregulation of PKB/Akt activity. This subsequently reduced the level of apoptosis signal-regulating kinase (ASK), and led to the activation of caspases 9. Altogether, our data demonstrate that SARS-CoV M-protein induces apoptosis through depriving PDK1 from interacting with PKB/Akt, this causes the activation of apoptosis. Our work highlights the SARS-CoV M protein is highly pro-apoptotic and is capable of simultaneously inducing apoptosis via initiator caspases 9.

Ref. No.: 08070492

P65-Ab0010

Comparable Fitness and Transmissibility between Oseltamivir-Resistant Pandemic 2009 and Seasonal H1N1 Influenza Viruses with the H275Y Neuraminidase Mutation

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Introduction: Neuraminidase (NA) inhibitors are one of the limited options for the control of influenza. The H275Y NA mutation, which confers resistance to oseltamivir carboxylate, was initially considered to be of little clinical consequence due to limited detection of this mutation in field isolates prior to 2007-2008, when a globally spreading H275Y variant emerged. Oseltamivir-resistant A(H1N1)pdm09 viruses with the H275Y NA mutation has been reported since 2009 but have not replaced the oseltamivir-sensitive wild-type strains to date.

Objectives: We aim to evaluate the effect of the H275Y NA mutation on fitness and transmission potential of three antigentically representative influenza strains of H1N1 subtype circulated among humans from 1999 to present time.

Methods: We generated recombinant viruses of different hemagglutinin (HA)-NA combinations and compared their growth in differentiated human airway epithelial cells that naturally secret mucin. The effects of the H275Y mutation on the NA enzyme activity of the seasonal and pandemic H1N1 viruses were determined using kinetic assays. The transmission potential of the recombinant viruses were evaluated using the ferret model.

Results: The H275Y mutation led to reduced NA enzyme activity, an decreased affinity for 3'-sialylactose or 6'-sialylactose substrates, and decreased infectivity in mucin-secreting human airway epithelial cells compared to the oseltamivir-sensitive wild-type counterparts. All H275Y variants of recombinant A(H1N1) pdm09 or seasonal H1N1 influenza viruses with different HA-NA gene constellations transmitted from inoculated ferrets to naïve direct contact or respiratory droplet contact ferrets, with the transmission efficiency minimally affected when compared to their wild-type counterparts.

Discussion: Our results suggest that the H275Y mutation in H1N1 influenza leads to minor reduction in viral fitness with its transmission potential being minimally affected in the naïve ferret model.

Ref. No.: 10090142

P66-Ab0011

Hemagglutinin–neuraminidase Balance Confers Respiratory-Droplet Transmissibility of the Pandemic H1N1 Influenza Virus in Ferrets

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Introduction: A novel reassortant derived from North American triple reassortant (TRsw) and Eurasian (EAsw) swine influenza viruses acquired sustained human-to-human transmissibility and caused the 2009 influenza pandemic. To understand the mechanism of the emergence of influenza pandemicity, it is essential to identify viral determinants that confer efficient transmission in humans.

Objectives: To evaluate the transmissibility of the pandemic H1N1 and its precursor swine influenza viruses in ferrets and to identify gene segments that confer to efficient respiratory droplet transmissibility.

Methods: Representative swine influenza viruses of different lineages were evaluated for direct-contact and respiratory droplet transmissibility in ferrets. Transmission is defined by detection of virus shedding from the naïve ferrets and sero-conversion. Plasmid-based reverse genetics was applied to introduce gene segments from pandemic H1N1 virus into selected precursor swine influenza virus to identify molecular determinants that confer transmissibility.

Results: All swine viruses studied were transmitted by direct contact with varying efficiency, respiratory droplet transmissibility (albeit inefficient) was observed only in the A/swine/Hong Kong/915/04 (sw915) virus, which is a TRsw-like that had acquired the M gene derived from EAsw and differed from the gene constellation of the pandemic H1N1 virus by the neuraminidase (NA) gene alone. Glycan array analysis showed that pandemic H1N1 virus A/HK/415742/09 (HK415742) and sw915 possess similar hemagglutinin (HA) receptor binding specificity and affinity for alpha2,6-sialosides. Introducing the NA from pandemic HK415742 into sw915 increased respiratory-droplet transmissibility; the NA of the pandemic virus possessed significantly higher enzyme activity than that of the sw915 or other swine influenza viruses.

Conclusions: Gene constellation and the HA-NA balance were the key determinants of the efficient human transmissibility of pandemic H1N1 viruses.

Implications: The results highlight the importance of continued swine influenza surveillance and the viral transmissibility evaluation in the ferret model for public health risk assessment.

Ref. No.: HK-09-02-05

P67-Ab0012

A Randomized, Parallel, Controlled Study to Evaluate the Role of Directly Observed Therapy Short Course-plus (DOTS-Plus) Versus DOTS for Retreatment of Pulmonary TB in Guangzhou

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Objectives: 1) To evaluate the outcomes and effectiveness in the retreatment of pulmonary TB by the use of conventional sputum culture and drug susceptibility testing (DST) in guiding chemotherapy under usual program conditions in Guangzhou and 2) study the factor(s) influencing outcomes in the retreatment of pulmonary TB under program conditions in Guangzhou. We hypothesized that the addition of conventional sputum culture and

DST for guiding subsequent modification of the standard World Health Organisation regimen for retreatment cases under the directly observed therapy-short course (DOTS) approach would lead to improved outcomes.

Methods: A prospective, randomized, parallel, open-labelled, controlled study comparing the outcomes and effectiveness of DOTS-plus with the addition of conventional sputum culture and drug susceptibility testing (DST) for guiding subsequent chemotherapy versus DOTS alone using the currently recommended standard 8-month regimen in the retreatment of smear-positive pulmonary TB under program conditions in Guangzhou.

Results: Altogether 114 and 111 were randomized into the DOTS and DOTS-Plus groups respectively. This report examined the initial outcome at 12 months after the initiation of chemotherapy. Using an intention-to-treat analysis (n=114 vs 111) and modified intention to treat analysis (n=81 vs 77) (excluding cases involving non-TB mycobacteria (NTM) and those with culture confirmation of TB at baseline, we found no significant differences in the overall proportion of favourable outcomes (cure / successful treatment completion) between DOTS and DOTS Plus. Among the multidrug-resistant TB (MDR-TB) cases, (n=13 vs 10), there was also no difference in the outcomes at 12 months between the two groups, and the estimated duration of infectiousness (up to the start of sustained culture conversion) did not differ materially. The slow turnover time for conventional culture and DST was a key factor limiting the field performance of DOTS-plus, with unnecessary initiation of treatment for false-positive sputum smears caused by NTM and failure or delay in staring definitive treatment incorporating secondline drugs for MDR-TB.

Conclusions: DOTS-plus utilizing conventional culture and DST did not perform better than DOTS in the retreatment of pulmonary TB under program settings in Guangzhou. Diagnostic tools with a shorter turnover time than these conventional tools are required to detect TB and MDR-TB to make a material difference in the fields.

Ref. No.: CHP-PH-10

P68-Ab0013

Automated Identification of Medically Important Bacteria by 16S rRNA Sequencing Using a Novel Comprehensive Database 16SpathDB

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Introduction: Rapid and accurate interpretation of 16S rRNA gene sequence results is the cornerstone for identification of medically important bacteria by 16S rRNA gene sequencing. However, interpretation of 16S rRNA gene sequence results is one of the most difficult problems faced by clinical microbiologists and technicians, despite the wide range of software and databases available. For example, as a result of the large number of unvalidated 16S rRNA gene sequences in GenBank, it is often not easy for inexperienced users to decide whether the "first hit" or "closest match" is the real identity of a bacterial isolate. As for the other software and databases, the usefulness is further limited by the choice of bacterial species in the database. If a bacterial species is not included in the database, it would never be the identity of an isolate. If the database includes bacterial species with minimal difference in their 16S rRNA gene sequences and hence cannot be identified confidently by 16S rRNA gene sequencing, these may also give rise to wrong identification if the software just reports that the "first hit" or "closest match" is the

identity of the bacterium.

In view of these problems, we have developed our own database in 2005 for identification of medically important bacteria using 16S rRNA gene sequencing.

Aims: 1. To develop a user-friendly and comprehensive database, 16SpathDB, for accurate identification of medically important bacteria.
2. To evaluate the usefulness of 16SpathDB.

Methods: 1. Design of database by including the most representative 16S rRNA gene sequence of all medically important bacteria listed in the 9th edition of the Manual of Clinical Microbiology.
2. Evaluate the usefulness of 16SpathDB: 16S rRNA sequence of 250 non-duplicated medically important bacterial isolates we collected in our clinical microbiology laboratory in the past 10 years were input to the database for analysis.

Results: 1. 16SpathDB is available at no charge at http://147.8.74.24/16SpathDB. As of April 2013, the database contained 1240 16S rRNA gene sequences from 1231 unique bacterial species.
2. All 250 bacteria recovered in our clinical microbiology laboratory were successfully identified using 16SpathDB.

Conclusions: We built a comprehensive and user-friendly database, 16SpathDB (http://147.8.74.24/16SpathDB). In 2011, the 10th edition of the manual was published and 16SpathDB was updated accordingly. The updated 16SpathDB 2.0 is also freely available at the same link given above.

Ref. No.: 11101102

P69-Ab0016

Typing of Plasmids Encoding CTX-M Type Extended-Spectrum Beta-Lactamases

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Introduction: The CTX-M type extended-spectrum b-lactamase is emerging worldwide in many countries. The CTX-M-14 allele has spread globally and is now endemic in many Asian countries, including China, Japan, Korea and Thailand. In Hong Kong, our recent study demonstrated the community emergence of CTX-M as the predominant ESBL among urinary *E. coli* isolates from women. CTX-M-14 was detected in 88% of ESBL-producing *E. coli* isolates with diverse genetic background. In addition, we found that CTX-M-14 was the most common genotype among faecal isolates of ESBL-producing E. coli causing colonization in this locality.

Objectives: We characterized plasmids encoding CTX-M-14 β-lactamase originating from *Escherichia coli* isolates recovered from patients with uncomplicated cystitis or individuals with faecal colonization in 2002 to 2004, Hong Kong.

Methods: Plasmids carrying CTX-M-14 were studied by conjugation, replicon typing, S1 nuclease-PFGE and plasmid PCR- Restriction Fragment Length Polymorphism (RFLP). The complete sequence of pHK01, a 70 kb plasmid encoding CTX-M-14 from a *E. coli* strain was determined and the results compared with reference plasmids and aligned with GenBank data.

Results: The bla$_{CTX-M-14}$ plasmids could be transferred in 23 of 44 *E. coli* strains tested. Among the 23 transconjugants, the replicon types of the CTX-M-14 encoding plasmid were FII (n=13), I1-Ig (n=4), F1B (n=2), FII and I1-Ig (n=1), and K (80 kb, n=1) and undetermined (n=2). Plasmid, pHK01 (FII replicon) shares a high degree of homology to R100 except mainly for a 11 kb variable region containing bla$_{CTX-M-14}$ (with an upstream ISEcp1 and a downstream truncated IS903), an iron transport system, an outer membrane protein (malB, maltoporin) and a putative toxin-antitoxin plasmid stability system (yacABC). It was highly related to plasmids encoding bla$_{CTX-M-14}$ (pKF3-70) and bla$_{CTX-M-24}$ (pEG356) reported from mainland China in 2006 and Vietnam in 2007, respectively. Subtyping by a plasmid PCR-RFLP scheme showed that ten of the 14 FII plasmids originating from isolates collected by multiple laboratories exhibited either identical or highly similar profiles.

Conclusions: This study showed that narrow host-range FII plasmids play important roles in the dissemination of CTX-M-14. FII plasmids closely related to pHK01 have disseminated widely in the Hong Kong community.

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P70-Ab0018
Does Vancomycin MIC Creep Occur among our MRSA Blood Culture Isolates?

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Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major public health threat. For decades, the glycopeptides have been the treatment of choice for serious MRSA infections such as bacteremia and ventilator-associated pneumonia. This becomes more complicated since 1997 when the first vancomycin-intermediate *S. aureus* (MIC 8 mg/L) was reported in Japan. Although MRSA with intermediate or high level of resistance to vancomycin remains rare, several studies found that MRSA may be less likely to respond to vancomycin when the MIC was ≥4 mg/L. Accordingly, the CLSI lowered the vancomycin susceptibility breakpoint for *S. aureus* to ≤2 mg/L in 2006. Since MIC is traditionally determined by 2-fold serial dilutions and susceptibility information provided as percentages of susceptible or resistant, small incremental increases in vancomycin MIC within the susceptible range (MIC creep) with time may go unrecognized.

Objectives: To assess whether vancomycin MIC creeps among blood methicillin-resistant Staphylococcus aureus (MRSA) isolates recovered from 5 hospitals in Hong Kong from 1997-2008.

Methods: Blood cultures MRSA isolates from 1997-1999 (period 1), 2004 (period 2) and 2006-2008 (period 3) were retrieved. Etest method was used to determine their vancomycin MIC. The genotypic features were determined by PCR and sequencing.

Results: 247 blood MRSA isolates were studied. The vancomycin MIC were 0.375, 0.5, 0.75 and 1 mg/L for 15 (6.1%), 68 (27.5%), 89 (36%) and 75 (30.4%) isolates, respectively. There was an increase in the percentage of isolates with an MIC = 1 mg/L from 10.4% (5/48) during period 1 to 21.6% (8/37) during period 2 and 38.3% (62/162) during period 3 (period 1 vs. period 3, P <0.001). Molecular typing showed that this was due to increased percentages of clonal cluster (CC) 8/SCCmec III/IIIA (agr group I), CC45/SCCmec IV/V (agr group IV) and other minor clones with

elevated MIC over time.

Conclusions: This study found vancomycin MIC creep among blood MRSA isolates over time. As elevated MIC within the susceptible range may reduce vancomycin efficacy, clinical laboratories should adopt methods with the required precision to accurately determine MICs.

Ref. No.: HK-09-01-04

P71-Ab0136
HBV Genotype-specific Mutations at Precore/core Region Affecting Intracellular Core Protein Localization and Viral DNA Synthesis

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Chronic infection of hepatitis B virus (HBV) greatly increases the risk of hepatocellular carcinoma (HCC). Mutations of the HBV genome at the core promoter and precore/core region are often related to more aggressive liver diseases and active hepatitis. Moreover, HBV core protein (HBcAg) expression pattern in hepatocytes could contribute to liver damage. Therefore, it is worthy to investigate if HBV genome mutations could affect the distribution of HBcAg in hepatocytes. In our previous work, several HBV subgenotype Cs specific hot spot mutations have been identified at core promoter (G1613A), precore region (G1899A), and the core gene (T2170G and T2441C). In this study, a total of thirteen 1.3x replication competent HBV clones harboring either single or multiple mutations were constructed. Then, effects of core gene mutations on intracellular HBcAg distribution and viral protein and DNA synthesis were investigated. By using confocal microscopy, the localization of HBcAg in hepatocytes was examined. Surprisingly, T2170G and T2441C could affect the intracellular localization of HBcAg to cytoplasm and nucleus, respectively. The phenotype caused by T2170G mutation could be observed in other mutants with combined mutations. Moreover, the secreted HBe antigen (HBeAg) was remarkably down-regulated in G1613A (90%) and T2170G (50%) mutants. Furthermore, enhanced viral DNA synthesis could be observed in G1613A and G1899A mutants, while T2170G mutant slightly decreased the viral DNA production in the culture medium. In conclusion, our results suggested that the mutations would affect the cytoplasmic/nuclear distribution of the HBcAg, HBeAg secretion and DNA synthesis. This may correlate to the more active viral pathogenesis and HCC progression.

Ref. No.: 09080302

P72-Ab0030
Cationic Amphipathic D-Antimicrobial Peptides as New Antituberculosis Agent

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Introduction and Aims: Tuberculosis (TB) control efforts have taken on increased urgency due to the emergence of multidrug-resistance (MDR). Current treatment of MDR-TB is lengthy (typically over 20 months) and is associated with severe adverse effects. There is an urgent need to develop a safe and effective anti-TB agent to combat the drug-resistant TB. Antimicrobial

peptides (AMPs) have the ability to target microbial pathogens within eukaryotic cells. In the present study, we aimed to investigate the activity of a series of structurally related AMPs, D-LAK peptides, against Mycobacterium tuberculosis (Mtb) including the drug-resistant strains.

Methods: The antituberculosis activities of six D-LAK peptides (with different hydrophobicity and structural conformation) were examined against clinical isolates of drug susceptible and MDR-Mtb using broth micro-dilution assay in 96 well plates. The cytotoxicity of the D-LAK peptides on human macrophage-like cells (THP-1) was examined by lactate dehydrogenase (LDH) and 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide) (MTT) assays. Furthermore, the effect of the combination of isoniazid and D-LAK peptides was also evaluated against MDR-TB.

Results: All the D-LAK peptides tested could successfully inhibit the growth of Mtb in vitro to a certain extent against MDR-TB. D-LAK peptides effectively dispersed the clumping of mycobacteria, consistent with the 'detergent-like effect' that could reduce the hydrophobic interactions between the highly lipidic surface of the mycobacteria, preventing bacteria cell aggregation. Although D-LAK peptides could not eradicate Mtb at non-toxic concentrations, they were effective as adjunct agent at low concentrations to potentiate the efficacy of isoniazid against drug-resistant Mtb without inducing cytotoxicity to mammalian cells, possibly by improving the uptake of the hydrophilic isoniazid into the mycobacteria by enhancing the surface permeability of the pathogen.

Conclusions: Out of the six tested D-LAK peptides, D-LAK120-A was identified as the optimal peptide within the peptide series based on the balance between the anti-TB activity against MDR-TB and the low cytotoxicity towards mammalian cells. Although D-LAK peptides alone may not be sufficiently potent at their non-toxic concentrations as the sole anti-TB agent, they could be used in combination with other anti-TB agents to improve their efficacy against drug-resistant TB. This combination approach could potentially improve the treatment against MDR-TB and reduce the adverse effects caused by the anti-TB drugs by lower their effective concentrations, leading to the improvement of patient compliance and treatment outcome.

Ref. No.: 11100682

P73-Ab0032
Characterization of Novel Anti-HIV/TB Natural Product Analogues

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Nonnucleoside reverse transcriptase inhibitors (NNRTIs) are one of the key components of antiretroviral therapy drug regimen against human immunodeficiency virus type 1 (HIV-1) replication. We previously described a newly synthesized small molecule, 10-chloromethyl-11-demethyl-12-oxo-calanolide A (F18), a (+)-calanolide A analog, as a novel anti-HIV-1 NNRTI (H. Xue et al., J. Med. Chem. 53:1397-1401, 2010). Here, we further investigated its antiviral range, drug resistance profile, and underlying mechanism of action. F18 consistently displayed potent activity against primary HIV-1 isolates, including various subtypes of group M, circulating recombinant form (CRF) 01_AE, and laboratory-adapted drug-resistant viruses. Moreover, F18 displayed distinct profiles against 17 NNRTI-resistant pseudoviruses, with an excellent potency especially against

one of the most prevalent strains with the Y181C mutation (50% effective concentration, 1.0 nM), which was in stark contrast to the extensively used NNRTIs nevirapine and efavirenz. Moreover, we induced F18-resistant viruses by in vitro serial passages and found that the mutation L100I appeared to be the dominant contributor to F18 resistance, further suggesting a binding motif different from that of nevirapine and efavirenz. F18 was nonantagonistic when used in combination with other antiretrovirals against both wild-type and drug-resistant viruses in infected peripheral blood mononuclear cells. Interestingly, F18 displayed a highly synergistic antiviral effect with nevirapine against nevirapine-resistant virus (Y181C). Furthermore, in silico docking analysis suggested that F18 may bind to the HIV-1 reverse transcriptase differently from other NNRTIs. This study presents F18 as a new potential drug for clinical use and also presents a new mechanism-based design for future NNRTI.

Ref. No.: 09080772

P74-Ab0132
Clostridium difficile Diarrhea: Risk Factors for Development and Recurrence

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Introduction: Clostridium difficile infection is a major cause of antibiotic-associated diarrhoea. Epidemiological studies in Western countries have shown a rapidly increasing incidence; nevertheless, limited epidemiological data are available in Asia.

Methods: We conducted a prospective case-control study comprising more than 140 cases and 110 controls in an acute-care hospital in Hong Kong. Clinical variables including patient characteristics, antibiotics history, concomittant medications and severity of the C. difficile infection, as well as microbiological variables including the ribotypes, antimicrobial susceptibility and toxin levels were studied.

Results: Compared to control subjects, patients with C. difficile infections had a longer hospital stay (20.4 vs 14.0 days, p<0.01) and a higher 60-day mortality (25.7% vs 12.0%, p<0.01). They were also more likely to have received proton-pump inhibitors (OR=2.21, 95%CI=1.28-3.86, P<0.01) or fluoroquinolones (OR=2.64, 95%CI=1.07-6.96, P=0.024) compared with the controls. The major ribotypes found were 002 (23%), 012 (14%) and 014 (14%). The ribotype 002 carried a mortality of 50%, and was shown to have a significantly higher toxin titre.

Conclusions: C. difficile infection in Hong Kong is associated with high morbidity and mortality. Risk factors include recent antibiotics exposure and use of acid suppressant. Our findings have major implications on disease prevention and control.

Ref. No.: CU-09-03-04

P75-Ab0034
Prevalence and Predictors of Maternal Seasonal Influenza Vaccination in Hong Kong

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Background: Pregnant women infected with influenza virus are

more likely to experience severe complications when compared with their non-pregnant peers. Yet influenza vaccine uptake is low among pregnant women. The purpose of this study was to assess the prevalence of seasonal influenza vaccine uptake among pregnant women in Hong Kong and to identify predictors of vaccine uptake.

Methods: Using a multi-center cross-sectional design, we recruited 2822 new mothers during their immediate postpartum stay from all eight public obstetric hospitals in Hong Kong. We assessed antenatal maternal influenza vaccination status as well as health beliefs and perceptions toward influenza and influenza vaccination. Bivariable and multivariable logistic regression was used to identify the predictors of vaccination uptake.

Results: Only 49 (1.7%; 95% CI 1.3-2.3%) participants were vaccinated during their pregnancy. Fear that the vaccine would cause harm to the fetus or themselves were the most common reasons for not being vaccinated. Being aware of the vaccination recommendations (OR = 2.69; 95% CI 1.06-6.82), being advised by a health-care provider (OR = 6.30; 95% CI 3.19-12.46), history of vaccination (OR = 2.47; 95% CI 1.25-4.91), perceived susceptibility to influenza infection (OR = 3.67; 95% CI 1.64-8.22), and perceived benefits of influenza vaccination (OR = 9.98; 95% CI 3.79-26.24) were all independently associated with vaccination. Perceived barriers to vaccination (OR = 0.17; 95% CI 0.07-0.40) were strongly associated with failure to vaccinate.

Conclusions: Low seasonal influenza vaccination uptake among Hong Kong pregnant women was related to a number of factors, all of which are amenable to interventions. Vaccination promotion strategies need to focus on encouraging health-care providers to discuss vaccination with their pregnant clients and in providing pregnant women with accurate and unbiased information about the risks of influenza infection and the benefits of vaccination.

Ref. No.: 10090982

P76-Ab0037
Influenza-like Illness and Viral Aetiology in Hong Kong Children

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Background: Respiratory viruses are responsible for thousands of hospitalizations and deaths every year in Hong Kong. However, there are few studies on the patterns in incidence of specific respiratory viruses in the community. The objectives of our study were to characterise the incidence rates of common respiratory viruses in children that lead to clinical presentation with ILI at primary care providers in the local community setting, and to compare our findings from primary care settings with inpatient data.

Methods: We recruited patients with acute respiratory illness from outpatient clinics across Hong Kong between 2007 and 2010. A nose and throat swab specimen was collected from each participant and stored at -70°C. In the present study, we tested those stored specimens for 18 respiratory viruses using the xTAG RVP FAST multiplex assay.

Results: We tested specimens from 2,090 specimens collected from eligible pediatric outpatients during the four-year study period, among which 1,343 (64%) were positive for any respiratory virus, and 81 (6%) specimens were found with more than one virus. The most frequently detected viruses were entero/rhinovirus (23.4%)

and influenza A (19.6%). Compared to outpatients, detection of RSV, parainfluenza, adenovirus and bocavirus was more common in inpatients in some age groups.

Conclusions: Respiratory viruses are frequently detected in pediatric outpatients in Hong Kong and the non-influenza viruses together appear to be associated with a much greater burden on ambulatory care than influenza A and B viruses. The increased detections of RSV, parainfluenza, adenovirus and bocavirus among inpatients suggest that these viruses may be associated with more severe illnesses than influenza and rhinovirus particularly.

Ref. No.: 10091272

P77-Ab0038
Effectiveness of Vaccinating Children in Reducing Influenza Among Household Contacts: A Community-based, Randomized Controlled Trial

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Background: Seasonal influenza vaccination is effective in preventing influenza infection and disease in healthy school-age children. Vaccinating a substantial proportion of children in a community can lead to indirect benefits via herd immunity, but less is known about the household-level indirect benefits of influenza vaccination of children. Moreover, the effectiveness of seasonal vaccine is unclear against a pandemic virus that was not included in the vaccine. The aim of this study was to estimate the direct effectiveness of 2009-10 seasonal trivalent inactivated influenza vaccine (TIV) in preventing influenza infection and illness in children aged 6-17, and the indirect effectiveness in preventing infection and disease in their household contacts.

Methods: A cluster-randomized trial in 796 households recruited between August 2009 and February 2010. One child in each household was randomized to receive 2009-10 seasonal TIV or saline placebo. Households were followed up for approximately 1 year. Sera were collected from all household members at the beginning and end of the study, and also collected from vaccine recipients one month after vaccination, and from 25% of all participants in April 2010. Households reported acute respiratory illness episodes in daily symptom diaries and biweekly telephone follow-up, and home visits were arranged to collect respiratory specimens during illness episodes. The primary outcomes were influenza infection confirmed by reverse transcription polymerase chain reaction (RT-PCR) or serologic testing by hemagglutination inhibition assay.

Results: Children who received TIV had reduced risk of seasonal influenza B confirmed by RT-PCR with vaccine effectiveness estimate of 66% (95% confidence interval, CI: 31%, 83%). Children who received TIV also had reduced risk of influenza B and pandemic influenza A(H1N1) confirmed by serology, with vaccine effectiveness estimates of 83% (95% CI: 46%, 95%) and 47% (95% CI: 15%, 67%) respectively. There was no significant difference in risk of influenza A and B virus infections among household contacts of children who received TIV or placebo. No serious adverse events were reported following vaccination, and most reported reactions to TIV were mild and local to the injection site.

Conclusions: Seasonal TIV had moderate effectiveness in preventing pandemic influenza A(H1N1) and influenza B infection. Indirect benefits were not observed in household

contacts. The potential mechanism for seasonal TIV to protect against pandemic A(H1N1) infection despite apparently poor immunogenicity deserves further study.

Ref. No.: CHP-CE-03

P78-Ab0039
Estimating the Effective Reproductive Number of Pandemic Influenza in Real-time

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Background: Timely estimation of the transmissibility of a novel pandemic influenza virus was a public health priority in 2009.

Methods: We extended methods for prospective estimation of the effective reproduction number, (R_t), over time in an emerging epidemic to allow for reporting delays and repeated importations. We estimated R_t based on case notifications and hospitalizations associated with laboratory-confirmed pandemic (H1N1) 2009 virus infections in Hong Kong from June through October 2009.

Results: We estimated that R_t declined from around 1.4-1.5 at the start of the local epidemic to around 1.1-1.2 later in the summer, suggesting changes in transmissibility perhaps related to school vacations or seasonality. Estimates of R_t based on hospitalizations of confirmed H1N1 cases closely matched estimates based on laboratory-confirmed case notifications.

Conclusions: Real-time monitoring of the effective reproduction number is feasible and can provide useful information to public health authorities for situational awareness and calibration of mitigation strategies.

Ref. No.: HK-09-04-02

P79-Ab0040
Optimal Design of Influenza Transmission Studies

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Background: Approximately one third of influenza virus infections are thought to occur in households, and this confined setting is often selected for studies of influenza transmission dynamics. Various design choices have been made in previous studies, but there has been limited discussion of optimal study design. Selecting an appropriate study design is part of Good Clinical Practice and use of suboptimal designs could squander research funding and put participants at unnecessary risk and inconvenience.

Methods: We used a simulation approach parameterized with data from household transmission studies to evaluate alternative study designs. We compared studies that relied on self-reported illness among household contacts versus studies that used home visits to collect swab specimens for virologic confirmation of secondary infections, allowing for the trade-off between sample size versus intensity of follow-up given a fixed budget.

Results: For studies estimating the secondary infection risk, 2-3 follow-up visits with specimens collected from all members regardless of illness were optimal. However, for studies comparing secondary infection risks between two or more groups, such as controlled intervention studies, designs with reactive home visits following illness reports in contacts were most powerful, while a

design with one home visit optimally timed also performed well.

Conclusions: Our results would suggest that given a reasonable cost per home visit, the use of home-visits is a cost-effective strategy as compared to relying solely on clinical diagnosis of influenza from self-report data. If resources for home visits were limited, acute respiratory illnesses with certain case definitions could be used to trigger home visits and this method performs well.

Ref. No.: HK-10-04-01

P80-Ab0041
Infectivity of Seasonal and Pandemic Influenza

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Background: There is limited information on the literature on how infectivity of persons infected with influenza virus varies over time in the same person, and how much variability exists between infected individuals. Estimates of changes in infectivity over time would inform control measures such as isolation and return-to-school (or work) policies, while information on heterogeneity between persons could improve models of transmission dynamics.

Methods: We enrolled outpatients with at least two signs or symptoms of acute respiratory illness, and used a rapid diagnostic test to identify patients with influenza virus infection. Those positive on the rapid test were further followed up with nose and throat swabs at enrolment and again after 3 and 6 days. We considered viral shedding measured by RT-PCR in the pooled nasal and throat swabs as a proxy for infectiousness and explored the heterogeneity of infectiousness among patients, and used linear mixed models to estimate variability within and between patients.

Results: In total, 637 patients had influenza A virus detected by a rapid test between 3 January 2008 and 28 August 2009, and 204 and 130 were subsequently confirmed to have seasonal A(H1N1) and A(H3N2) infection, respectively. Compared with adults, children shed a similar amount of virus at illness onset, with a longer overall duration and slower rate of decline. There was greater variability in virus shedding among children, compared with adults, particularly for seasonal A (H1N1). The top 20% most infectious children and adults were estimated to be responsible for 89%--96% and 78%--82%, respectively, of the total infectiousness in each age group.

Conclusions: Our analysis revealed that viral shedding is more heterogeneous in children than in adults. On the assumption that shedding is a proxy of infectiousness, the higher level and longer duration of shedding in children are consistent with the notion that children are more infectious than adults. Further investigation is required to correlate the substantial variations in viral shedding with heterogeneity in actual transmissibility.

Ref. No.: HK-10-04-02

P81-Ab0134
Insights from the Complete Genome Sequence of Mycobacterium Tuberculosis Beijing Genotype on Microevolution Proneness for Population Expansion and Drug Resistance

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The Beijing genotype of Mycobacterium tuberculosis (MTB) has received much attention due to its growing worldwide prevalence, hypervirulence and predisposition to multidrug resistance. We have sequenced complete genomes of five Beijing isolates, including two far beyond the current drug resistance standard - a "Totally Drug Resistance" (TDR) phenotype. The significance of these high-quality genomes is five-fold. The better mapping performance over H37Rv genome when employing Beijing genotype sequence reads argues favorably a useful resource for large MTB Beijing genotype research community. Similar ratio of non-synonymous to synonymous substitutions to previously reported mean in MTB Complex suggests that mechanisms other than point mutations alone may be driving adaptation. Considering variations in both region of difference (RD) and non-synonymous suggests that membrane proteins and transposable elements are different in Beijing and non-Beijing genotypes. A novel marker that differentiates Beijing from non-Beijing genotype in the "modern" MTB was identified, revealing previously unnoticed evolutionary relationship. Expansion of repetitive and non-repetitive sequences scattered in the genome signifies host-focused population expansion. In TDR strains big deletions and truncations events were more frequently found in genes that are retained in the genome of the extremely-slow growing Mycobacterium leprae.

Ref. No.: 08070502

P82-Ab0044
The Attack Rate, Transmission Dynamics and Viral Evolution in a Cohort of Hong Kong Families during an Epidemic of Novel Influenza Virus (H1N1)

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Background: Before the 2009 human swine influenza pandemic, we were conducting a pilot cluster randomized controlled trial of seasonal influenza vaccine in reducing household transmission of influenza. At the beginning of the pandemic, little was known about its attack rates, effectiveness of seasonal influenza vaccine and genomic information regarding the pandemic strain. The objective of this study was to assess the age-specific community attack rates, effectiveness of seasonal influenza vaccine and genomic information regarding the 2009 human swine pandemic influenza strain.

Methods: One child 6–15 years of age from each of 119 households was randomized to receive 1 dose of inactivated trivalent seasonal influenza vaccine (TIV) or saline placebo in November 2008. Serum samples were collected from study subjects and their household contacts before and 1 month after vaccination (December 2008), after winter (April 2009) and summer influenza (September–October 2009) seasons. Seasonal and pandemic influenza were confirmed by serum hemagglutinination inhibition, viral neutralization titers, and reverse-transcription polymerase chain reaction performed on nasal and throat swab samples collected during illness episodes. RT-PCR-positive swabs were cultured, and isolates were sequenced to provide genetic data on locally circulating pandemic viruses.

Results: TIV recipients had lower rates of serologically confirmed seasonal A/H1N1 infection (TIV 8%, placebo: 21%; p=0.10) and A/H3N2 infection (7% vs 12%; p=0.49), but higher rates of serologically-confirmed pandemic A/H1N1 infection (32% vs 17%; p=0.09). Age-specific seroprevalence rate was highest in young household contacts in TIV group (TIV 6-15y 33%; 16-44y 13%; ≥45y 12% vs placebo 6-15y 18%, 16-44y 12%, ≥45y 11%). In multivariable analysis, individuals who were infected with seasonal influenza A during the study period had a lower risk of laboratory-confirmed pandemic A/H1N1 infection (adjusted odds ratio=0.35; 95% CI: 0.14-0.87), and receipt of seasonal TIV was unassociated with risk of pandemic A/H1N1 infection (adjusted OR=1.11; 95% CI: 0.54-2.26). Genetic sequencing confirmed that clusters of cases within households were closely related (i.e. confirming within-household transmission), and no antiviral-resistant viruses were identified.

Conclusions: A substantial proportion of children and young adults were infected during the first wave of 2009 pandemic. Vaccination against seasonal influenza protected against strain-matched infection in children. Naturally acquired seasonal influenza infection appeared to confer cross-protection against pandemic influenza. Whether prior seasonal influenza vaccination predisposes to a higher risk of infection with the pandemic strain requires confirmation.

Ref. No.: PHE-2

P83-Ab0045
Flagship Collaboration Project: Surveillance Surveys on Population-based Responses to Human Swine Influenza in Hong Kong

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Background: Previous studies of severe acute respiratory syndrome (SARS) highlighted the need for the promotion of preventive measures to take into account background perceptions of risk and anxiety, because higher perceived risk of infection was more likely to lead to an increase of precautionary measures against infection. Little is known about the community psychological and behavioral responses to influenza pandemics.

Methods: Using random digit dialing, we sampled 12,965 Hong Kong residents in 13 cross-sectional telephone surveys between April and November 2009, during the first wave of the 2009 influenza A(H1N1) pandemic. We examined trends in anxiety, risk perception, knowledge on modes of transmission, and preventive behaviors.

Results: Respondents reported low anxiety levels throughout the epidemic. Perceived susceptibility to infection and perceived severity of H1N1 were initially high but declined early in the epidemic and remained stable thereafter. As the epidemic grew, knowledge on modes of transmission did not improve, the adoption of hygiene measures and use of face masks did not change, and social distancing declined. Greater anxiety was associated with lower reported use of hygiene measures but greater social distancing. Knowledge that H1N1 could be spread by indirect contact was associated with greater use of hygiene measures and social distancing.

Conclusions: The lack of substantial change in preventive measures or knowledge about the modes of H1N1 transmission in the general population suggests that community mitigation measures played little role in mitigating the impact of the first wave of 2009 influenza A(H1N1) pandemic in Hong Kong.

Ref. No.: PHE-1&10 (HKU)

P84-Ab0047
Behavioural Changes in Relation to Risk Perception and Prevention of Avian and Human Influenza in the General Population of Hong Kong, 2006 to 2010

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Background: The Hong Kong government has introduced a series of progressive measures on importation, farming and retail of live poultry to minimize risk of A/H5N1 transmission since 1997. Perceived risk of A/H5N1 and related preventions could decline as these macro-level policies minimizing human-chicken contact. This may paradoxically increase population risk of other influenza and respiratory infection due to reduced preventive behaviors.

Objectives: A follow-up survey in 2010 was conducted to investigate change of live poultry exposure, risk perception and prevention of A/H5N1 among respondents who participated in the random household telephone survey in 2006.

Methods: Totally, of 1,760 respondents who completed the 2006 survey, 680 could be traced and 461 (68%, 461/680) agreed and completed the repeated telephone survey between July and August 2010. Prevalence of buying and touching, perceived risk of A/H5N1, worry, and protective hygiene practices were compared between 2006 and 2010 using descriptive analysis. How changes of these variables differed by respondents' demographics and change of perceived risk and worry leaded to change of buying and practices of hygiene were further explored by multivariate logistic regression analyses.

Results: Prevalence of household buying live poultry declined from 73% in 2006 to 41% in 2010. Buying household bought on averaged 11.4 chicken/household/year in 2010 versus 14.4 in 2006 while touch rate remained unchanged (5%). Overall exposure (touch rate × purchase rate) declined by 21% from 2006 to 2010 (0.72 vs. 0.57 exposure/household/year). Most personal hygiene practices improved from 2006 to 2010 except that frequency of daily hand-washing and covering mouth when sneezing and coughing declined. Male respondents reported less likely to cover mouth when sneezing or coughing (OR=1.60, 95%CI: 1.00-2.56) while immigrants were more likely to report reduced frequency of daily hand-washing (OR=1.58, 95%CI: 1.04-2.41). Perceived risk from buying live poultry and worry about contacting A/H5N1 declined from 2006 to 2010. Younger respondents were more likely to report declined worry and risk from buying live poultry. Declined worry was associated with less hygiene practices (OR=1.61, 95%CI: 1.04-2.47).

Conclusions: The decline in buying prevalence may be attributed to limiting poultry availability. However, among buyers, prevalence of touching poultry remained unchanged, suggesting little effect from public health promotion to change purchasing-related behaviours. Perceived risk from buying, A/H5N1 worry and some hygiene practices declined, suggesting that risk of contracting human influenza viruses could increase. Young males and immigrants should be the major target for public health education to promote hygiene practices.

Ref. No.: 09080732

P85-Ab0050
Mass Spectrometrical Identification of Host Cell Surface Protein Receptor(s) for Human Norovirus in Primary Human Duodenal Tissues

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Introduction: Human noroviruses (NoVs), a member of the family Caliciviridae in the genus Norovirus, is the leading cause of acute non-bacterial gastroenteritis worldwide which affects all age groups in both developed and developing countries. Our understanding on the pathogenesis of NoV has been severely hampered by the lack of a robust in vitro cell culture system and small animal model for NoV. We believe identifying candidate host cellular receptor(s)/co-receptor(s) for NoV may provide important data to the direction of developing an in vitro cell culture system. Laboratory investigations of natural NoV infections and volunteer challenge studies have demonstrated NoV-associated histopathological changes in human small intestines. However, direct evidence showing viral antigens in infected intestinal epithelial cells has been lacking. This raises the concern whether NoV infects enterocytes.

Methods: In this study, we first used in vitro whole-virus binding assay to study NoV tissue tropism. Total protein lysate of human duodenal biopsy specimens were then subjected to virus overlay protein binding assay (VOPBA) and mass spectrometry to identify candidate host cellular receptor(s)/co-receptor(s).

Results:
1. Using in vitro whole-virus binding assay, human norovirus genogroup II genotype 4 (NoV GII.4) Sakai strain was found to bind to human duodenal lamina propria and Brunner's glands.
2. Using virus overlay protein binding assay (VOPBA) and mass spectrometry on total protein lysate of human duodenal biopsy specimens, nucleolar protein 8 (NOL8) was identified as a candidate host cellular protein receptor/co-receptor for NoV GII.4 Sakai strain.
3. NoV may target intestinal non-epithelial cells.

Conclusions: We provide evidence that NoV GII.4 Sakai strain showed in vitro binding pattern to duodenal lamina propria and Brunner's glands, but not to epithelial enterocytes. NoV may target intestinal non-epithelial cells. NOL8 may be a candidate cellular receptor/co-receptor for NoV and deserves further investigations.

Ref. No.: CU-09-02-05

P86-Ab0052
Identification of Hepatitis B Virus DNA Polymerase Sequences to Predict Virological Response to Entecavir Therapy

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Background and Aims: Entecavir is a potent antiviral agent that often reduces hepatitis B virus (HBV) DNA to an undetectable level after one year of treatment, but HBV DNA may remain detectable in some patients. We aimed to determine whether baseline HBV reverse transcriptase (rt) sequence polymorphism

and quasispecies complexity and diversity were associated with treatment response.

Methods: Pre-treatment HBV DNA levels, HBV rt sequence, and serology from a cohort of 305 entecavir-treated patients were determined. Quasispecies complexity and diversity were determined by clonal sequencing and analyzed using MEGA software. These data were tested for the association with year one virological outcome, defined by optimal response (undetectable HBV DNA; ≤12 IU/mL) or partial response (detectable HBV DNA).

Results: Four rt variants were more frequently detected in the 64 partial responders than in the 241 optimal responders (43.8-51.6% vs. 20.1-27.4%, all P < .05). Multivariate analysis revealed that high baseline HBV DNA (P < .0001; odds ratio [OR] = 2.31), hepatitis B e antigen (HBeAg)-positivity (P < .001; OR = 3.68) and rt124N (P = .001; OR = 3.09) were associated with partial entecavir response. Molecular docking model suggested that rt124N possibly cause a slight steric hindrance to entecavir binding. Compared with the optimal responders, the partial responders had a lower quasispecies complexity and diversity at both the nucleotide and amino acid levels.

Conclusions: Apart from the known factors (high baseline HBV DNA, HBeAg-positivity), a novel single nucleotide polymorphism (rt124N) and lower quasispecies complexity and diversity were associated with partial entecavir response at year 1. Identification of these viral factors can assist in choosing an optimal antiviral treatment for individual patients.

Ref. No.: 08070852

P87-Ab0053

Application of Co-amplification at Lower Denaturation Temperature-PCR (COLD-PCR) Sequencing for the Early Detection of HBV Antiviral Drug Resistant Mutations

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Background and Aims: Nucleoside/nucleotide analogue for the treatment of chronic hepatitis B virus (HBV) infection is hampered by the emergence of drug resistance mutations. Conventional PCR-sequencing cannot detect minor variants of <20%. We aimed to develop a modified CO-amplification at Lower Denaturation temperature-PCR (COLD-PCR) method for the detection of HBV minority drug resistance mutations. During thermal-cycle of COLD-PCR, the denaturation temperature (normally at 95°C) was reduced to a lower-than-normal critical denaturation temprature. Using a critical denaturation temperature, minor variants can be enriched during PCR.

Methods: The critical denaturation temperature for COLD-PCR was determined using real-time PCR. Sensitivity of COLD-PCR sequencing was determined using serially-diluted plasmids containing mixed proportions of HBV reverse transcriptase (rt) wild-type and mutant sequences. The performance of COLD-PCR sequencing was compared to that of conventional PCR-sequencing and a line probe (LiPA) assay, using 215 samples obtained from 136 lamivudine- or telbivudine-treated patients with virological breakthrough.

Results: The critical denaturation temperature for COLD-PCR was 78°C. With serially-diluted mixture of wild-type and rt mutant plasmids as templates, conventional PCR-sequencing detected mutations only if they existed in ≥25%, whereas COLD-PCR sequencing detected mutations when they existed in 5-10% of

the viral population. Among the 215 clinical samples obtained from the lamivudine- or telbivudine-treated patients, drug resistance mutations were detected in 155 (72 %), 148 (69 %) and 113 samples (53 %) by LiPA, COLD-PCR, and conventional PCR-sequencing, respectively. Nineteen (9 %) samples had mutations detectable by COLD-PCR but not LiPA, while 26 (12 %) samples had mutations detectable by LiPA but not COLD-PCR, indicating both methods were comparable (P = 0.371). COLD-PCR was more sensitive than conventional PCR-sequencing: 35 (16 %) samples had mutations detectable by COLD-PCR but not conventional PCR-sequencing, while none had mutations detected by conventional PCR-sequencing but not COLD-PCR (P < 0.0001).

Conclusions: COLD-PCR sequencing is a simple method which is comparable to LiPA and superior to conventional PCR-sequencing in detecting minor lamivudine/telbivudine resistance mutations.

Ref. No.: 09080682

P88-Ab0058

Effect Modifications of Lifestyle Factors on Risk of Mortality Associated with Influenza in an Elderly Cohort

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Background: Influenza has been associated with a heavy burden of mortality and morbidity. The prevention strategy relies on vaccines and antiviral drugs, while there have been few studies which tackled the effects of healthy lifestyle on influenza to provide evidence for promoting an adjunctive approach.

Aims and Objectives: To assess the effects of smoking, alcohol drinking and exercise on influenza associated mortality risks and address the role of health lifestyle as adjuncts to vaccination and antiviral medication in prevention of influenza.

Methods: We collected the baseline lifestyle information of 66,820 persons aged 65 or above recruited by18 Elderly Health Centers (sample fractions 6.5 - 17.2%) in Hong Kong from May 1998 to December 2001. The subjects were followed up for health outcomes till December 2009, by anonymously linking the death records of deceased subjects to the baseline data. Effect modification of each lifestyle factor on influenza associated excess mortality risk from all-natural and cardiorespiratory causes was assessed by time-dependent Cox proportional hazard model. The mortality excess risks associated with influenza for categories of each lifestyle factor were also separately assessed by stratified analysis.

Results: We found that influenza associated mortality risks were higher in ex- and current-smokers compared to never smokers, and the associations were particularly high in female smokers (Wong et al. 2013). Compared to never-drinkers, ex-drinkers had a higher while social/regular drinkers had a lower excess risk associated with influenza. Among the exercise groups, sedentary people had a higher and frequent exercisers had a lower excess risk associated with influenza. An U-shape pattern across the underweight, normal, overweight, moderate obesity and severe obesity groups was observed in influenza associated mortality risks (Yang et al. 2012).

Conclusions and Implications: Maintaining healthy lifestyle is associated with reduction of mortality risks attributable to influenza. Health education to promote cigarette smoke quitting and regular exercise shall be integrated with other preventive measures against influenza.

Ref. No.: 09080532

P89-Ab0060
Spatio-temporal Modelling for Early Detection of H1N1 Pandemic Influenza Outbreak in Hong Kong

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Background: The outbreak of SARS a decade ago placed Hong Kong in a solemn and alienated situation. Fear of infectivity and uncertainty about its risk location were the major causes of community panic. The concept of applying mathematical models for disease surveillance was undeveloped at the time. There was also the limitation of significant time lag in using disease case statistics reported by frontline clinicians in disease surveillance. Although a number of temporal models were available for disease surveillance, having a spatio-temporal model would illustrate the geospatial pattern of disease spread to identify infection clusters in different communities of Hong Kong. Using data about H1N1 outbreak and governed by the susceptible-exposed-infected-removed (SEIR) epidemiological structure, this study gathered essential map data for the development of a spatio-temporal model that offers visualisation of spatial diffusion patterns with forecast ability.

Methods: The study examined 216 confirmed cases of H1N1 influenza from 1 May 2009 to 20 June 2009 within the urban setting of Hong Kong to develop the stsSEIR (spatio-temporal and stochastic SEIR) forecast model. Line graphs and similarity maps were used to assessed the 1-7 day forecast accuracy and spatial forecast accuracy respectively.

Results: The 1-7 day forecast line graphs showed that the stsSEIR model could predict the H1N1 influenza outbreak 1 to 2 days in advance with very high R^2 values of 0.79 and 0.8 respectively. The accuracy decreased with increasing number of forecast days in advance. Relatively small R^2 values of 0.52 and 0.36 were observed respectively for 6 and 7 day advance forecasts. The similarity maps showed the model was able to predict the location of disease clusters with over 80% error free cells, although some cells reported errors of 3 or more cases. These cells with higher error counts, however, coincided with the actual locations of local outbreaks albeit of different intensity.

Conclusions: A novel spatio-temporal mathematical model for detecting locations of H1N1 influenza outbreak has been developed for Hong Kong. This model has been validated for 1 to 2 day advance forecast subject to a minimum number of 5 initial cases. We have demonstrated that the model can serve as a spatial predictive model for Hong Kong to forewarn the H1N1 influenza outbreaks by their geographic location.

Ref. No.: 10090122

P90-Ab0065
Feasibility and Pilot Findings of Repeated Nasopharyngeal Sampling for Influenza Surveillance in Hong Kong Preschool Children

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Background and Objectives: Influenza is one of the major viral respiratory infections in children, which readily spread by aerosol transmission through close contact within children's families and classes. However, local epidemiological data from inpatient and outpatient sources only includes cases with obvious respiratory symptoms. There is limited surveillance data for the full spectrum of influenza infections within the school setting, due partly to questionable feasibility of repeated sampling of respiratory samples from young children. This prospective study aimed to investigate the feasibility of collecting periodic nasopharyngeal swabs in local preschoolers, and obtained pilot data of influenza incidence among these young children.

Methods: Fifty-four 5-year-old children were recruited from three randomly selected kindergartens in Shatin and Ma On Shan districts. Their parents completed a questionnaire on demographics, health status and influenza vaccination. Nasopharyngeal flocked swabs (NPFSs) were collected during: (i) 2-weekly surveillance school visits during one influenza season between February and March 2012 and (ii) illness visits for children with respiratory infections. Influenza A and B viruses was detected by multiplex polymerase chain reactions.

Results: Forty-nine of 54 consented children gave at least one NPFS, and 44 (89.8%) of them provided four surveillance NPFS samples. Thirteen samples from 12 (24.5%) children were influenza-positive, including 10 (20.4%) of 49 children by surveillance and 3 of 10 sick children. Only two (16.7%) children were vaccinated within 12 months. Influenza was not associated with any environmental or vaccine-related factors.

Conclusions: Repeated nasopharyngeal sampling is a feasible approach for influenza surveillance among local preschool children. A significant proportion of these children with influenza infection have minimal respiratory symptoms. Low influenza vaccine uptake is also common in young local children.

Ref. No.: 11100482

P91-Ab0066
A Feasibility Study on the Inhibition of Swine Influenza A Virus H1N1 Infection Using siRNAs with a Unique Motif

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The 2009 pandemic influenza A virus H1N1 has raised concerns of more severe influenza pandemic in future. Although current antiviral drugs - Tamiflu and Relenza, are still effective for the treatment of this emerging infectious disease, rapid emergence of drugs-resistant virus has been reported, which would result in the failure of the treatment in short future. In previous study, we have found that siRNAs containing a unique motif can induce strong b-defensin-4 production in mouse respiratory tract, which can efficiently inhibit infections of influenza virus and other respiratory viruses. In this study, we aimed to develop effective prophylatic and therapeutic agents against the H1N1 influenza using siRNAs with

the motif. Our study results showed that (1) eight of 58 designed siRNAs could significantly suppress viral replication in cell cultures at IC50 around or less than 25 µM; (2) a lethal H1N1 virus infection mouse model was successfully established; (3) the previous effective siRNA delivery system PEG8/PEI1.8 failed to deliver siRNAs into cells of animal respiratory tract in this study, which might be due to that it was stored for more than 3 years; (4) the rAAV-shRNAs could significantly inhibit H1N1 virus replication in cell cultures, but failed to provide effective protection against lethal challenge of H1N1 virus in mouse model, because the rAAV could not infect and deliver the shRNAs to the target cells, i.e. epithelial cells of the conducting airways, bronchi and bronchiole in the mice; and (5) alternately, the expressed functional b-defensin-4, synthesized full length b-defensin-4 lineated peptide and one (P9) of short peptides derived from b-defensin-4 were demonstrated to be able to significantly inhibit the infection of H1N1 virus in cell cultures, while the P9 could provide potent protection against lethal challenge of the H1N1 virus in the mouse model. The knowledge gained in this study will lay a foundation for developing specific and effective antiviral agents against pandemic H1N1 influenza and also provide useful information for rational design and development of nucleic acids and antiviral peptides for prophylaxis and therapy of other emerging viral infectious respiratory diseases.

Ref. No.: HK-09-02-03

P92-Ab0067

Cross-protective Efficacy of Immunization with Different Forms of M2 Vaccines and their Combinations with HA Vaccines against Highly Pathogenic H5N1 Influenza A Viruses in Mice

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Recent outbreaks of H5N1 avian influenza virus that causes severe diseases in humans have raised concerns over an imminent influenza pandemic. As yet, there is no effective and universal vaccine that could be used to prevent and combat H5N1 infection. In this regard, development of vaccines for the prevention of H5N1 avian flu is an urgent need. In this study, we aims to develop universal vaccine based on different forms of M2 vaccine candidates and their combinations with HA against H5N1 infection. We designed and prepared mM2e (synthetic monomer M2e peptide), M2e-MAP (tetra-branched multiple antigen peptide), fusion protein M2e-ASP-1 (1 M2e fused with ASP-1) and M2e3-ASP1 (3 M2e fused with ASP-1), DNA-M2, rAAV-M2, DNA-HA, rAAV-HA, protein HA and inactivated virus vaccine. We tested immune responses and protective effects of these vaccine candidates, as well as effects of different aduvants. Our results showed that (1) M2e-MAP, M2e-SAP-1 and M2e3-ASP-1 elicited much stronger M2e-specific antibody responses than M2e, DNA-M2 and rAAV-M2; (2) M2e-MAP and M2e3-ASP-1 provided better protection and cross-protection against viral challenges of different clades/strains of H5N1 virus and H1N1 virus than M2e-ASP-1, whereas mM2e, DNA-M2 and rAAV-M2 did not show obvious protection against viral challenge of H5N1 virus; (3) consistently, the mice vaccinated with M2e-MAP and M2e3-ASP-1 showed much lower viral load detected and less inflammation found in lung tissues; (4) cross-protective effect of M2e-based vaccines might be related to the identity of the M2e sequence between the vaccine and the H5N1 virus; (5) rAAV-HA, DNA-HA and inactivated virus vaccine provided effective protection against infection of homologous H5N1 virus, whereas these vaccine candidates and protein HA provided poor cross-protections against heterologous H5N1 viral infection; and (6) combination vaccinations with M2e-based and HA-based vaccine candidates, particularly vaccination of both M2e-MAP

and inactivated virus vaccine, provided potent cross-protection against challenges with heterologous strains of H5N1 virus. Taken together, this study has demonstrated that both M2e-MAP and M2e3-ASP-1 can provide potent cross-protection against infections of some heterologous strains of H5N1 virus and H1N1 virus, while the strategy of combination vaccinations with both HA-based and M2e-based vaccines may be able to improve the cross-protection against heterologous H5N1 virus infection. Therefore, this study has provided the theoretical and practical basis for development of effective and universal vaccines against H5N1 influenza virus infection.

Ref. No.: 09080812

P93-Ab0068

Co-administration of Antiviral and Anti-inflammatory Agents against Avian Influenza Virus H5N1 Infection in Animal Model

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Patients with H5N1 infection frequently progress to severe pneumonia and acute respiratory distress syndrome, resulting in very high mortality. Antiviral therapy such as oseltamivir is likely to be effective as prophylaxis and at early stage but not thereafter. This lack of therapeutic efficacy at the later stage of illness may be often attributed to a cytokine storm, once triggered by the virus, becomes a self-propagating local and systemic inflammatory response despite that the viral infection is controlled by antivirals. In this study, we tested our hypothisis that delayed cocktail treatment of antiviral and anti-inflammatory can effectively reduce the pulmonary damage and thus save patient's life in H5N1 viral infection animal model. Our results showed that (1) Zanamivir showed higher antiviral effect than Ribavirin and Nucleozin, while cocktail treatment of these antiviral agents did not show significant synergistic antiviral effect; However, delayed zanamivir therapy reduced survival rate of viral challenged mice significantly. (2) Treatments of single non-COX-2 immunomodulator, i.e. artesunate, steroids, gemfibrozil, kaletra, flufenamic acid, aprotinin, n-acetylcysteine and mucosolvan (ambroxol), did not increase survival rates in the infected animals, but the treatment of flufenamic acid, aprotinin, mucosolvan and n-acetylcysteine prolonged the survival time of mice for 3.3, 2.9, 2.1 and 1.8 days, respectively. (3) Cocktail treatments of non-COX-2 anti-inflammatory agents flufenamic acid, aprotinin, mucosolvan and n-acetylcysteine did not show significant synergistic protective effect in the infected mice. (4) Cocktail treatments using COX-2 inhibitor (celecoxib) and non-COX-2 agents (aprotinin, mucosolvan and n-acetylcysteine) did not show significant synergistic protective effect, but the cocktail treatment of COX-2 inhibitor celecoxib and non-COX-2 agent flufenamic acid further prolonged the survival time of the mice to 4.2 days. (5) Delayed cocktail treatments of antiviral (zanamivir) and COX-2 inhibitors (celcoxib and mesalamine), non-COX-2 agent (flufenamic acid), or celcoxib and flufenamic acid significantly improved survival in mice challenged with H5N1 virus as compared with the survial in mice received delayed antivial therapy alone. The survival benefits of adding celecoxib and mesalazine, flufenamic acid, or celecoxib and flufenamic acid to zanamivir could be due to their synergistic effects in reducing cytokine dysfunction, suppressing inflammatory responses and preventing apoptosis. Cocktail treatments of antiviral and these COX-2 and non-COX-2 immunomodulators should be considered in randomized controlled treatment trials of patients suffering from H5N1 infection.

Ref. No.: 09080762

P94-Ab0069
Functional Characterization of Candida Albicans Apoptosis-Inducing Factor

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Introduction and Objectives: Apoptosis is a highly organized cellular process crucial for growth and development. Apoptosis has been demonstrated in unicellular yeast Saccharomyces cerevisiae, but little is known in opportunistic human fungal pathogen Candida albicans. Previous studies showed that typical apoptotic features could be induced in C. albicans.

Mitochondria are Bifunctional Organelles: they are energy powerhouse; but also set a central stage that leads to cell demise. Mitochondrial dysfunction has been regarded as the onset of apoptosis, manifested by depolarization of mitochondrial membrane potential (MMP), massive elevation of ROS, and release of apoptosis-inducing factor (AIF) and cytochrome c. Translocation of AIF from mitochondrial intermembrane space to nucleus causes chromatin condensation, DNA cleavage and cell death. No C. albicans AIF has been identified so far.

We previously revealed that purpurin causes MMP depolarization without significant increase in intracellular ROS levels in Candida fungi, suggesting an existence of a mitochondrial-mediated cell death pathway. Searching the published C. albicans genome using S. cerevisiae AIF, we have identified three putative AIF sequences (orf19.1438, orf19.2175 and orf19.2671). The objectives of this project were:
1. To clone and express the three putative C. albicans AIF sequences; and
2. To determine the cellular localization and function role of AIF in energy production and cell death.

Methods: The three putative C. albicans AIF sequences were cloned by PCR, expressed and purified from Escherichia coli BL21 as His-tag fusion proteins (CaAifp). Chromosomal green fluorescent protein-tagged AIF was constructed to detect cellular localization using confocal microscopy. The NADH oxidase activity of the purified CaAifp was determined by spectrophotometric method; and the cell death-related functions of the CaAifp were evaluated by examining sub-cellular translocation after apoptotic insults, ability to degrade DNA, and complementation to S. cerevisiae Δaif1 mutant.

Results: The three putative C. albicans AIF sequences were cloned, expressed and purified to homogeneity from E. coli BL21 (i.e. CaAifp-orf19.1438, CaAifp-orf19.2175 and CaAifp-orf19.2671). CaAifp-orf19.2175 and CaAifp-orf19.2671 possessed NADH oxidase activity. CaAifp-orf19.2175 degraded DNA and functionally complemented S. cerevisiae Δaif1 mutant.

Conclusions: The collective data of the present study suggest that orf19.2175 encodes a bona fide C. albicans AIF and the AIF-mediated cell death mechanism in C. albicans shares phylogenetic conservation to that in S. cerevisiae. Deciphering C. albicans AIF paves way for the elucidation of additional effector molecules in the mitochondrial-mediated cell death pathway and also casts light on the design of anti-Candidal strategy by promoting cell suicide.

Ref. No.: 11101122

P95-Ab0070
Transmission Dynamics of Scarlet Fever in Hong Kong

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Introduction: Scarlet fever, caused by Group A Streptococcus (GAS) bacterium, is mainly transmitted via direct contact with saliva and nasal fluids from infected persons. Many children may also carry GAS or be asymptomatically infected. Scarlet fever is a notifiable disease in Hong Kong, mainland China and Macau, and all three areas reported substantial increases since 2011.

Methods: We provided basic descriptive epidemiological data on scarlet fever and calculated the maximum cross-correlations between spline-interpolated weekly notifications in Guangdong and Macau versus that in Hong Kong. We estimated the instantaneous reproduction number (R_t) which measures the time dependent frequency of transmission per single primary case.

Results: In 2011, a total of 1526 cases (21.6 per 100,000 population) with 730 laboratory confirmed and 46 imported cases were reported in Hong Kong, almost ten times the average annual notifications in the preceding 10 years. Among which, there were 2 fatal cases (a 7 year-old girl and a 5 year-old boy). Most of the reported cases were under 10 years old (range: 1 month-51 years) with a median age of 6 years.

There were elevated scarlet fever notification rates in New Territories East (NTE), New Territories West (NTW), Kowloon (KL) and Hong Kong Island (HKI), at 27.2, 21.7, 18.9 and 19.6 per 100,000 population, respectively. There were significantly higher proportions of the imported cases before July 2011 (12 out of the 14, p-value for exact binomial test = 0.01) in NTE and NTW where the main border crossings to mainland China are located. Maximum cross-correlations between spline-interpolated weekly scarlet fever notifications in Guangdong and Macau versus that in Hong Kong were found at 1 and 2-week lags respectively (ρ=0.45 and 0.58). R_t was consistently above 1 from mid-May through the end of June, but fell quickly below 1 since early July after reporting of two fatal scarlet fever cases which raised widespread concern in the community.

Conclusions: The correlation between cases in Hong Kong, Guangdong and Macau is suggestive of a link to the outbreak in Guangdong during the early phase of the local outbreak. Step-up surveillance, publicity and health education to the public, guidance on prevention and control measures were implemented by Centre for Health Protection in early June and could have contributed to the reduction in transmissibility. Efficient cross-border communication and timely sharing of epidemic information, and maintaining public awareness will be beneficial in the control of scarlet fever.

Ref. No.: HK-11-04-02

P96-Ab0071
Genome Sequence Analysis Platform for Identification of Genetic Determinants and Development of Molecular Markers for Diagnosis of Human Systemic Infection by Salmonella Enterica Serovar Typhimurium

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Salmonella enteric serovar Typhimurium is frequently isolated from foodborne infection cases in Hong Kong, but the lack of genome sequences from local isolates have hindered in-depth epidemiological and phylogenetic studies. We aimed to investigate genetic variations, identify determinants for systemic infection, to reconstruct phylogenetic relationship among local S. Typhimurium clinical isolates using their genome sequences, and to develop and evaluate molecular markers of diagnostic value.

In this study, genome sequences of 10 local S. Typhimurium clinical isolates were resolved using 454 GS-FLX Titanium genome sequencer. Taken together 10 other local clinical isolates previously resolved, there are totally 7 blood isolates and 13 stool isolates. Genomic and virulent elements including Salmonella Pathogenicity Islands (SPIs), virulence factors, tRNAs, small non-coding RNAs, prophage elements and CRISPRs structures were annotated. Bioinformatics analyses were employed to investigate genetic variations and identify potential determinants for Salmonella systemic infection. Phylogenetic analysis revealed that the 20 sequenced local isolates could be grouped into two distinct phylogenetic clades. The two clades revealed an observable difference in their virulence potential. Nevertheless, explicit determinants of human systemic infection had not been concluded, despite the aerobactin siderophore was revealed as a potential system that favours intracellular bacterial growth. Molecular markers were identified to differentiate the two different clades as well as to detect for the presence of the aerobactin system. The markers could be used to differentiate more virulent isolates from less virulent ones as shown with additional clinical samples.

This study demonstrated the potential application of the genome sequence analysis platform in the differentiation of pathogenic infectious bacteria. New phylogenetic clades of S. Typhimurium strains may be emerging and attention should be paid before their virulence level and pathogenicity are known.

Ref. No.: 10090432

P97-Ab0073
The Application of Interferon Gamma Release Assay in the Assessment of Latent Tuberculosis Infection among Healthcare Workers in Hong Kong

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Introduction and Objectives: In-vitro interferon gamma release assay (IGRA), including QuantiFERON-TB Gold In-Tube (QFT-GIT), is a specific marker for the diagnosis of latent tuberculosis infection (LTBI). We investigated its application in contact investigations for healthcare workers.

Methods: We performed a two-year prospective cohort study. Healthcare workers were recruited from QEH, UCH, and PMH between Jan-2010 and Jun-2011. Blood specimens for QFT-GIT were taken from patients exposed to smear-positive TB patients, on recruitment, 3 months, 6 months and 12 months.

Results: 159 exposed and 120 non-exposed participants were recruited. Baseline QFT-GIT positivity is associated with age ≥ 40 (RR 1.62, 95% CI: 1.23 - 2.11), and working as healthcare workers for ≥ 10 years (RR 1.44, 95% CI: 1.15-1.79).

Using cut-off (0.35IU/mL), QFT-GIT conversion from negative to positive blood tests at three months was 8.85% (10/113) for

exposed group and 4.54% (4/88) for non-exposed group. RR: 1.30 (95% CI: 0.91 - 1.85). There was no difference in conversion at study end between two groups.

When a grey zone of between (0.2 IU/mL to 0.7 IU/mL) was implemented, QFT-GIT conversion at 3 months was 2.97% (3/101) for exposed group and 1.03% (1/79) for non-exposed group. RR 2.347 (95% CI 0.249, 22.129).

Conclusion and Discussion: This is the largest scale TB contact investigation study using IGRA for healthcare workers in Hong Kong. The local prevalence of LTBI is now found to be 20.7% in our cohort.

QFT-GIT conversion after clear TB exposure history was most implicated as new acquisition of TB infection. 3 months was regarded as the time required for TST conversion. Our findings suggest a tendency of QFT-GIT conversion after TB exposure within three months, albeit not statistically significant.

Our study failed to obtain significant result as we have a few QFT-GIT converters. This can be explained by our relatively loose inclusion criteria. Only 52.7% of our index patients have AFB smear 3+, and the mean duration of exposure was only 27.08 hours. On the other hand, the association of QFT-GIT conversion with active TB disease was not found, due to the short follow-up duration. Further studies with longer term serial monitoring are warranted.

Ref. No.: 09081002

P98-Ab0076
Complete Genome Analysis of Drug-susceptible and Multidrug-resistant Pseudomonas Aeruginosa

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Pseudomonas aeruginos is a significant source of bacteraemia in burn victims, urinary-tract infections in catheterized patients and hospital-acquired pneumonia in patients on respirators. These infections are difficult to eradicate and can ultimately lead to pulmonary failure and death. Notably, multidrug resistance in Pseudomonas aeruginosa is steadily increasing worldwide. In this study, genomes of four Pseudomonas aeruginosa strains (two drug-susceptible strains - PA753236 and PA83365 and two multidrug-resistant strains - PA123036 and PA185388) have been sequenced, assembled and annotated. We have analyzed our genomes together with eight genomes (PAO1, 19BR, 213BR, DK2, LES431, LESB58, M18, MTB-1, NCGM2.S1, PA1, PA1R, PA7, RP73, SCV20265, YL84, PACS2) downloaded from NCBI. Phylogenetic analysis of these 16 genomes has been done using the housekeeping genes (acsA, aroE, guaA, mutL, nuoD, ppsA and trpE). A comparison of multidrug-resistant strains and drug-susceptible strains were done with PAO1 as background. Totally, 5,703 SNPs were reported that only exists in the multidrug-resistant strains. Among them, 1,047 out of 4,757 SNPs in the coding regions were non-synonymous mutations, involving 584 genes. Functional analysis by DAVID suggests that those genes participated in diverse biochemical processes. It is also interesting that we identified two plasmids (around 420kb and 530kb in size) similar to the Pseudomonas

aeruginosa plasmid pOZ176. Sequencing reads corresponding to these plasmids could only be found in drug resistant strains but not in susceptible strains. We hypothesize that these plasmids may also contribute to the drug-resistant feature of the Pseudomonas aeruginosa.

Ref. No.: CU-09-05-03

P99-Ab0077
Identification of Genomic Variations and Gene Network in Multidrug-resistant Acinetobacter Baumannii

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Acinetobacter spp. are important nosocomial pathogens associated with hospital-acquired infections. In hot, humid areas, such as Hong Kong, Acinetobacter infection is endemic, with higher incidences of nosocomial infection than those reported elsewhere. Institutional outbreaks caused by Acinetobacter baumannii (AB) strains that have acquired multiple mechanisms of antimicrobial drug resistance constitute a growing public-health problem. Notably, outcomes of patients with Acinetobacter baumannii infections seem to be poorer if caused by isolates with resistance to multiple classes of antimicrobial agents. In this study, the genomes of two AB resistant strains exhibiting very high resistance to carbapenems (imipenem and meropenem MICs > 32 μg/ml), fluoroquinolones (ciprofloxacin, >32 μg/ml) and cephalosporins (ceftriaxone > 128 μg/ml and cefepime > 32 μg/ml), together with two drug sensitive strains, were determined by next generation sequencing platform. A phylogenetic tree was constructed and we found that our sequenced strains formed a separated cluster in the tree. Totally, 47 common non-synonymous mutations in 33 genes that are predominantly appeared in drug resistant strains were identified. The functional relationship of these genes were then investigated by bioinformatics tools including STRINGS and DAVID. Finally, we found that the folate pathway, SOS response, DNA repair and recombination system, and the drug efflux system may play an important role in the emergence of drug resistance in AB.

Ref. No.: CU-09-05-02

P100-Ab0079
Viral RNA Replication Kinetics Study and Host Early Inflammatory Cytokines Response Profiling of Human Norovirus Infection: An ex vivo Organ Culture Study

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Background: Human norovirus (hNoV) is a major cause of non-bacterial gastroenteritis worldwide in all age groups. However, the lack of a robust cell culture system for hNoV severely hampers the study of this important pathogen. Ex vivo virus culture, which mimics the in vivo microenvironment, may be an alternative approach to study hNoV.

Objectives: (i) Evaluation of ex vivo culture to support hNoV infection and replication, and (ii) study of temporal relationship of host early inflammatory cytokines response with hNoV replication

kinetics in ex vivo culture.

Methods: First, we used in vitro whole virus binding (IVWVB) assay to evaluate whether ex vivo culture of human duodenal tissues could become a viable model for hNoV infections. We then evaluated whether hNoV underwent productive RNA replication in ex vivo virus culture. Finally, we used array-based technology to profile gene expression of Th1 and Th2 cytokines upon hNoV infections in our ex vivo virus culture model.

Results: In IVWVB assay, hNoV was found to bind predominantly to cells of lamina propria and Brunner's glands of human duodenum. Productive noroviral RNA replication was observed in ex vivo virus culture. Upon hNoV infection ex vivo, there was a preferential down-regulation of cytokines and genes related to Th1 pathway whereas more genes associated with Th2 pathway were up-regulated.

Conclusions: Our findings suggest that ex vivo culture using human duodenal tissues is a viable model for the study of hNoV infection. Using our model, we demonstrate that hNoV infection may elicit predominant Th2 intestinal immune response in situ.

Implications: hNoV may display tropism to non-epithelial cells. This provides important insights into future direction of hNoV cultivation efforts. The predominant activation of Th2 pathway in ex vivo-infected human duodenal tissues implies that adaptive immune response may play a greater role in hNoV pathogenesis.

Ref. No.: 08070422

P101-Ab0080
Human Norovirus Structural Viral Protein 2 in the Emergence of Epidemic Variants

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Introduction: Human noroviruses (NoVs) are leading causes of sporadic cases and outbreaks of acute viral gastroenteritis in both developing and developed regions. During the past two decades, periodic emergence of novel NoVs belonging to the genogroup II genotype 4 (GII.4) lineage have been documented. The virion of NoVs is composed of two structural proteins: major viral protein 1 (VP1) and minor VP2. The protruding domain 2 (P2 domain) of VP1 has been shown to be continuously mutating during the virus evolution of the NoV GII.4 lineage. In contrast, sequence analysis studies on VP2 have been rare and it is interesting to know whether this minor structural protein undergoes similar rapid mutations in the virus evolution.

Methods: Time-ordered nucleotide sequence analysis, clonal sequencing, and yeast two-hybrid assay were used

Results:
1. In human norovirus genogroup II genotype 4 (NoV GII.4) lineage, nucleotide sequence hypervariability was observed in viral protein 1 (VP1)-interaction domain of VP2 on 3 levels: (1) during the global evolution of pandemic/epidemic strains from mid-1970s through post-2006; (2) during the local emergence of an epidemic strain; and (3) in an immunocompromised chronic shedder of NoV.
2. Using quantitative yeast two-hybrid assay, VP2 was found to interact with VP1 in a time-ordered strain-dependent manner among 3 NoV GII.4 strains.

Conclusions: We report that sequence hypervariablity is not only observed in VP1 (P2 domain) but also in VP2 (VP1-interaction

domain) of NoV GII.4 strains. Our findings indicate that VP2 co-varies with VP1 in the evolution of the NoV GII.4 lineage. Time-ordered strain-dependent interaction of VP1 and VP2 suggests that co-variation may be functionally driven. VP2 should be included in future sequence analysis studies of the NoV GII.4 lineage.

Ref. No.: CU-09-02-04

P102-Ab0082
Effects of Environmental Ventilation Characteristics on Exhaled Air Dispersion in the Operating Theatre

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Introduction: Ventilation systems in the operating theatre are designed to minimize the number of environmental particles within the room. It is unclear whether these systems affects the spread of potentially infected air particles from the patient to the surgeons, anesthetists and nurses during coughing. We compared the dispersion of exhaled air during coughing in operating theatres incorporated with non-laminar airflow ventilation; laminar airflow ventilation and negative pressure ventilation.

Methods: We used the high-fidelity Human Patient Simulator (HPS, Medical Education Technologies Inc, Sarasota, FL) to produce coughing bouts (0.2 s). Expiratory airflow were adjusted to represent cough in patients with normal (500 L/min) and moderate (250 L/min) or severe (150 L/min) lung injury.1,2 Exhaled air was marked with oil-based smoke particles of ≤ 1 μm in diameter, introduced to the right main bronchus of the HPS. Exhalation jet was revealed by an intense laser light-sheet. Images of leakage plume were captured with high definition video camera. Normalized concentration of smoke in the exhalation jet was calculated according to a modified particle image velocimetry technique.

Results: A total of 9 scenarios were studied (3 ventilation systems with 3 coughing efforts). The downward displacement of laminar ventilation was effective in reducing the dispersion of exhaled air after coughing. Essentially, highly concentrated (80%) exhaled air was rapidly dispersed and diluted in laminar flow ventilation system (30 mm from the mouth of the HPS after strong cough in normal lung condition, 26 mm in moderate lung injury and 20 mm in severe lung injury). In contrast, the dispersion of exhaled air was > 100 mm in non-laminar flow ventilation system. Interestingly, room pressure (positive vs negative) has no significant effect on exhaled air dispersion.

Conclusions: In a simulated situation, we demonstrated that laminar flow over the operating table was effective in minimizing spread of exhalation air as the patient coughed. Positive or negative room pressure did not affect exhaled air dispersion.

Ref. No.: CU-10-01-02

P103-Ab0083
Institutional Risk Factors for Norovirus Outbreaks in Hong Kong Elderly Homes: A Retrospective Cohort Study

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Background: Most of the institutional outbreaks of norovirus (NV) in Hong Kong occur in elderly homes, the proportion being 69% in 2006. Residents in elderly homes are a special group seriously affected by NV infections.

Objectives: To study the in stitutional risk factors for NV outbreaks in Hong Kong elderly homes using a retrospective cohort study.

Methods: A cohort of 748 elderly homes was followed up from January 2005 to December 2007; each elderly home was treated as one observation unit and the outcome event was NV outbreak. Cox regression models were fitted to estimate the relative risk (RR) and 95% confidence interval (CI) for the potential risk factors.

Results and Conclusions: Elderly home capacity, staff-to-resident ratio and wheelchair accessibility were risk factors for NV outbreaks in Hong Kong elderly homes. Supply of partitions between beds was a protective factor. Attendant-borne transmission might be an important transmission mode in the elderly homes. These results should guide infection control policy in elderly homes.

Ref. No.: 08070452

P104-Ab0084
Exhaled Air Dispersion during Application of Common Respiratory Therapies at Prince of Wales Hospital Clinical Service Block and Princess Margaret Hospital Infectious Diseases Block

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Aims: We examined whether different isolation room dimensions and air exchange rates would have different performance in removing exhaled air from the patient.

Methods: We studied the exhaled air dispersion distances during a) oxygen delivery via nasal cannula to a human-patient simulator(HPS) at the Princess Margaret Hospital(room A) and the Prince of Wales Hospital(room B). Room A had a dimension of 4.1×5.1×2.6m, pressure -7.4Pa, and 16 air changes/hr(ACH) whereas room B had a dimension of 2.7×4.2×2.4m, pressure -5Pa and 12ACH. Additional experiments conducted in room A: b) during coughing±wearing a surgical or N95 mask; c) when the HPS was manually ventilated using a Laerdal Silicone Resuscitator± a viral bacterial filter. Airflow was marked with intra-pulmonary smoke for visualization. The leakage jet was revealed by laser and images captured by high-definition video. Smoke concentration in the plume was estimated from the light scattered by smoke particles and significant exposure was defined as where there was ≥20% of normalized smoke concentration.

Results:
a) Oxygen therapy via nasal cannula
Room A: An exhalation jet spread almost horizontally outward from the nostrils of the HPS to 0.66m and 1m towards the end of bed when oxygen flow was increased from 1 to 5 L/min respectively.
Room B: The downward ceiling ventilation current interacted with the exhaled air from the HPS, leading to deflection of exhaled smoke towards the head of the HPS at an oxygen flow rate of 1L/min. As oxygen flow was increased gradually to 5L/min, more room contamination with smoke was noted.
b) During normal cough efforts, the exhaled air dispersion distances were 68, 30, and 15cm along the median sagittal plane

when the HPS wore no mask, a surgical mask and a N95 mask whereas the lateral dispersion distances were 0, 28 and 15cm respectively.

c) During manual ventilation, the dispersion distance of the exhaled plume was 20cm through the expiration diverter along the sagittal plane whereas that in the transverse plane was 22cm. With addition of the filter, leakage from the expiration diverter was eliminated but the exhaled plume distance along the transverse plane increased to 34cm.

Conclusions: PMH isolation room is relatively more effective in removing exhaled air and preventing room contamination than PWH during application of oxygen therapy. N95 mask is better than surgical mask in reducing exhaled air during coughing. Viral bacterial filter can stop leakage through the expiratory diverter during manual ventilation but may increase sideway leakage.

Ref. No.: CU-09-01-05

P105-Ab0086
Knowledge, Attitudes, Practices, and Preparedness of Poultry Workers with Regard to H5N1 Avian Influenza

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Background: Zoonoses of H5N1 avian influenza from birds to humans virus poses the potential for a worldwide pandemic. Live poultry workers in Hong Kong are an occupational risk group that is at highest risk of infection and adverse sequelae.

Objectives: To describe the H5N1-related knowledge, attitudes, preventive and risk behaviours and outbreak preparedness and the associated factors.

Study Design: An anonymous, cross-sectional survey was conducted using an interviewer-administered questionnaire between June and November 2009.

Setting and Subjects: 360 live poultry workers from all 133 retail and 23 wholesale establishments in Hong Kong were sampled. Potential respondents were invited with $50 supermarket coupons as incentives after making assurance of confidentiality and anonymity.

Main Outcome Measures: The poultry worker's H5N1-related knowledge, their attitudes about the severity and susceptibility to avian influenza and the perceived barriers and benefits of adopting preventive measures are examined. Current poultry handling practices and preparedness in the event of an H5N1 outbreak were also analyzed.

Results: Live poultry workers exhibited noteworthy H5N1-related knowledge gaps. More than half of them believed that the disease is rarely fatal and nearly 90% believed that the virus could not be transported on clothing. This occupational group also demonstrated very low perceptions of H5N1 susceptibility with about half of them believing themselves to have immunity to H5N1 infection. Knowledge levels correlated strongly with the communication channels from which they obtained health information. Even after adjusting for socio-demographic factors, poultry workers who obtained H5N1 information from the internet and ancillary sources such as health talks or other poultry-workers demonstrated substantially higher knowledge. The main factor that was significantly associated with lower levels of preventive behaviors and lower levels of H5N1 preparedness was the perceived barriers to adopting these behaviors. Inaccessibility

of training and interference of preventive practices with work were cited as the main obstacles to greater compliance with infection control.

Ref. No.: 08070412

P106-Ab0088
Cost-Effectiveness of Pneumococcal Conjugate Vaccines in Hong Kong

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Introduction: In 2008, a cost-effectiveness model was developed to assess the cost/life year of the infant 7-valent pneumococcal vaccine (PCV-7) in Hong Kong. That vaccine was subsequently made available locally at a subsidized rate in 2009. Since then, two new vaccines have become available which cover more serotypes: the 10-valent (PHiD-CV) and 13-valent (PCV-13) vaccines.

Aims: To examine the cost-effectiveness of PHiD-CV and PCV-13 and to compare these with the cost-effectiveness of PCV-7 in Hong Kong.

Methods: The net costs of vaccinations were calculated as the cost of vaccination using the specific vaccine minus the saved costs of health and social care avoided due to vaccination from a societal perspective. A steady-state population model was used to estimate the impact of the three vaccines over a year in which the effects had reached a steady state. All data used was estimated by age group as far as possible. The serotype prevalence among cases of invasive pneumococcal disease (IPD) was summarised for the years prior to the availability of PCV-7 in Hong Kong and used to estimate the efficacy of the each vaccine according to the serotypes it contained. The burden of disease after vaccination with each vaccine was compared to a base year in which it was assumed there was no vaccination. The efficacy of the vaccines was based on empirical results from a US study of impact of PCV-7 and assumptions were made about the efficacy of the other two vaccines and about an indirect effect which included herd immunity and serotype replacement. Utility scores from overseas were used to value the life years and estimate quality-adjusted life years (QALYs) gained.

Results: The PCV-13 was the most cost-effective with a cost per QALY gained of HK$62,840. Varying assumptions about the vaccine effectiveness and the size of the indirect effect did not make much difference to the cost per QALY gained nor to the rank ordering of the vaccines. At the assumed price of HK$500 for the more cost-effective vaccine, PCV-7 would have to cost only HK$236 per dose to achieve the same level of cost-effectiveness as PCV-13, and PHiD-CV should only cost HK$251.

Conclusions: Under the assumptions made, PCV-13 would be more cost-effective than PCV-7 or PHiD-CV in Hong Kong at a cost per QALY gained of HK$62,840. This option is very cost-effective compared with a nominal value for a QALY of around HK$300,000.

Ref. No.: CHP-CE-10

P107-Ab0089
Harvesting Convalescent Plasma for Hyperimmune Intravenous Globulin Production: A Multicentre, Randomised Double-Blind Controlled Trial for Treatment of Patients with Serious S-OIV H1N1 Infection

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Background: Experience from influenza pandemics suggested that convalescent plasma treatment given within 4 to 5 days of symptom onset might be beneficial. However, robust treatment data is lacking.

Methods: This is a multicentre prospective double-blind randomized controlled trial. Convalescent plasma from patients who recovered from the 2009 pandemic influenza [A(H1N1) pdm09] infection was fractionated to hyperimmune intravenous immunoglobulin (H-IVIG) by CSL Biotherapies, Australia. Patients with severe A(H1N1)pdm09 infection on standard antiviral treatment requiring intensive care and ventilatory support were randomized to receive H-IVIG or normal IVIG manufactured before 2009 as control. Clinical outcome and adverse effects were compared.

Results: Between 2010 and 2011, thirty-five patients were randomized to receive H-IVIG (17 patients) or IVIG (18 patients). One defaulted patient was excluded from analysis. No adverse event related to treatment was reported. Baseline demographics and viral load before treatment were similar between the two groups. Serial respiratory viral load demonstrated that H-IVIG treatment was associated with significantly lower day 5 and 7 post-treatment viral load when compared to the control (p=0.04 and p=0.02 respectively). The initial serum cytokine level was significantly higher in the H-IVIG group but fell to similar level 3 days after treatment. Subgroup multivariate analysis of the 22 patients who received treatment within 5 days of symptom onset demonstrated that H-IVIG treatment was the only factor which independently reduced mortality [OR:0.14, 95% CI, 0.02-0.92; p=0.04].

Conclusions: Treatment of severe A(H1N1)pdm09 infection with H-IVIG within 5 days of symptom onset was associated with a lower viral load and reduced mortality.

P108-Ab0090
In Silico Structure-based Screening and Characterization of Inhibitors for Influenza A Virus Nucleoprotein

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The trend of drug resistance developed in different strains of influenza viruses is worrying, and it is of utmost importance and urgency to develop new drugs against this virus. The viral nucleoprotein (NP) is a major component of the ribonucleoprotein (RNP) complex for the transcription and replication of the virus. In order to maintain a stable RNP structure, NP forms homo-oligomers by inserting its tail-loop to the tail-loop insertion site of another NP. In this study, we have employed structure-based virtual screening on the influenza A NP tail loop insertion site and found two hit compounds number 7 and 16 that can subdue influenza RNP activities. Subsequently, two analogs from compound 16 were identified which inhibit RNP activities of various influenza A subtypes and viral growth at micromolar levels. These analogs were also shown to directly interact with NP at 12.0 ± 1.25 and 41.6 ± 1.93 µM respectively by surface plasmon resonance assay. These novel anti-influenza compounds would provide a template for designing drug candidates with higher potency.

P109-Ab0091
A Detailed Longitudinal Study of Infection Attack Rates among Healthy Adults in Hong Kong during the Epidemic of the Human Swine Influenza A/H1N1 Virus in 2009

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Background: In an emerging influenza pandemic, estimating severity (the probability of a severe outcome, such as hospitalization, if infected) is a public health priority. As many influenza infections are subclinical, sero-surveillance is needed to allow reliable real-time estimates of infection attack rate (IAR) and severity.

Methods and Results: We tested 14,766 sera collected during the first wave of the 2009 pandemic in Hong Kong using viral microneutralization. We estimated IAR and infection-hospitalization probability (IHP) from the serial cross-sectional serologic data and hospitalization data. Had our serologic data been available weekly in real time, we would have obtained reliable IHP estimates 1 wk after, 1-2 wk before, and 3 wk after epidemic peak for individuals aged 5-14 y, 15-29 y, and 30-59 y. The ratio of IAR to pre-existing seroprevalence, which decreased with age, was a major determinant for the timeliness of reliable estimates. If we began sero-surveillance 3 wk after community transmission was confirmed, with 150, 350, and 500 specimens per week for individuals aged 5-14 y, 15-19 y, and 20-29 y, respectively, we would have obtained reliable IHP estimates for these age groups 4 wk before the peak. For 30-59 y olds, even 800 specimens per week would not have generated reliable estimates until the peak because the ratio of IAR to pre-existing

seroprevalence for this age group was low. The performance of serial cross-sectional sero-surveillance substantially deteriorates if test specificity is not near 100% or pre-existing seroprevalence is not near zero. These potential limitations could be mitigated by choosing a higher titer cutoff for seropositivity. If the epidemic doubling time is longer than 6 d, then serial cross-sectional sero-surveillance with 300 specimens per week would yield reliable estimates when IAR reaches around 6%-10%.

Conclusions: Serial cross-sectional serologic data together with clinical surveillance data can allow reliable real-time estimates of IAR and severity in an emerging pandemic. Sero-surveillance for pandemics should be considered.

Ref. No.: PHE-20

P110-Ab0092
A Longitudinal Study of Infection Attack Rates among Hospital Outpatients in Hong Kong during the Epidemic of the Human Swine Influenza A/H1N1 Virus in 2009 by Tracking Temporal Changes in Age-specific Seroprevalence Rates

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Seroprevalence survey is the most practical method for accurately estimating infection attack rate (IAR) in an epidemic such as influenza. These studies typically entail selecting an arbitrary titer threshold for seropositivity (e.g. microneutralization [MN] 1:40) and assuming the probability of seropositivity given infection (infection-seropositivity probability, ISP) is 100% or similar to that among clinical cases. We hypothesize that such conventions are not necessarily robust because different thresholds may result in different IAR estimates and serologic responses of clinical cases may not be representative. To illustrate our hypothesis, we used an age-structured transmission model to fully characterize the transmission dynamics and seroprevalence rises of 2009 influenza pandemic A/H1N1 (pdmH1N1) during its first wave in Hong Kong. We estimated that while 99% of pdmH1N1 infections became MN1:20 seropositive, only 72%, 62%, 58% and 34% of infections among age 3-12, 13-19, 20-29, 30-59 became MN1:40 seropositive, which was much lower than the 90%-100% observed among clinical cases. The fitted model was consistent with prevailing consensus on pdmH1N1 transmission characteristics (e.g. initial reproductive number of 1.28 and mean generation time of 2.4 days which were within the consensus range), hence our ISP estimates were consistent with the transmission dynamics and temporal buildup of population-level immunity. IAR estimates in influenza seroprevalence studies are sensitive to seropositivity thresholds and ISP adjustments which in current practice are mostly chosen based on conventions instead of systematic criteria. Our results thus highlighted the need for reexamining conventional practice to develop standards for analyzing influenza serologic data (e.g. real-time assessment of bias in ISP adjustments by evaluating the consistency of IAR across multiple thresholds and with mixture models), especially in the context of pandemics when robustness and comparability of IAR estimates are most needed for informing situational awareness and risk assessment. The same principles are broadly applicable for seroprevalence studies of other infectious disease outbreaks.

Ref. No.: 10090272

P111-Ab0093
Effectiveness of School Closures for Pandemic Influenza

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Large-scale antiviral intervention is now a major component of influenza pandemic preparedness planning in many countries. The emergence and spread of antiviral resistance (AVR) can substantially attenuate the effectiveness of large-scale antiviral intervention (e.g. targeted prophylaxis) and worsen the prognosis of severe cases (because antivirals will not be efficacious for cases infected with resistant strains). Reliable and timely estimates of the transmissibility of resistant strains is a public health priority once AVR is detected during an influenza pandemic.

Ref. No.: HK-09-04-01

P112-Ab0095
Direct Identification and Quantification of Host and Viral Transcriptomes after Influenza Infection Using the Next Generation Ultra-High Throughput DNA sequencer

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Introduction: Highly pathogenic avian influenza H5N1 virus causes lethal disease in humans. This virus can trigger a rapidly progressive viral pneumonia leading to acute respiratory distress syndrome. Studies from clinical, in vivo and in vitro data suggest a role of virus induced cytokine dysregulation in contributing to the pathogenesis of human H5N1 disease, however, the precise mechanisms by which the H5N1 virus elicits the differential and unique host responses are still not well understood.

Methods: To better understand the molecular events at the earliest time points, we used RNA-Seq to quantify and compare the host and viral transcriptomes induced by highly pathogenic H5N1 (A/Vietnam/3212/04) or low virulent H1N1 (A/Hong Kong/54/98) influenza viruses in human monocyte-derived macrophages at different post infection time.

Results and Conclusions: Our data revealed that our samples contained a variable mix of two macrophage populations corresponding to the M1 (classically activated) and M2 (alternatively activated) macrophage subtypes, a distinction not possible with previous microarray studies. When this confounding variable is considered in our statistical model, a clear set of dysregulated genes and pathways emerges at 6 hour post infection specifically in H5N1-infected macrophages, but not with H1N1 infection. Furthermore, we mapped reads comprise annotated known miRNA and found a distinct cellular miRNA expression patterns in response to influenza virus infection. We analyzed a set of potential miRNA target genes based on an inversely correlated expression pattern between the target mRNA and miRNAs and highlighted that innate immunity pathways particularly RIG-I like receptor signaling is significantly enriched in response to infection. In addition to known miRNAs, we have also identified some novel human miRNA species which have not been reported previously, while no miRNA was found to be encoded by influenza viruses.

Ref. No.: 08070532

P113-Ab0098
Helicobacter Pylori-induced STAT3 Activation and Signalling Network in Gastric Cancer

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Background: Helicobacter pylori (H. pylori) is the most important gastric carcinogen. However, the mechanisms of H. pylori induced gastric carcinogenesis through STAT3 activation are largely unknown. We evaluated the effects of H. pylori infection on STAT3 activation and dissected the signalling network of STAT3 in H. pylori-infected gastric carcinogenesis.

Methods: The expression of phospho-STAT3 (pSTAT3) was evaluated by immunohistochemistry and western blot. Gene expression array and chromatin immunoprecipitation were used to dissect the STAT3 signalling network on H. pylori co-cultured AGS.

Results: The STAT3 activation (pSTAT3) was significantly higher in H. pylori-positive gastritis (73.5%, 61/83) than in H. pylori-negative gastritis (50%, 35/70) (P = 0.003). In addition, 98% (43/44) of H. pylori positive intestinal metaplasia specimens showed STAT3 activation, whereas pSTAT3 was significantly decreased in all 43 specimens one year after H. pylori eradication (P < 0.001). Moreover, pSTAT3 was only detected in the H. pylori-infected gastric tissues of mice but not in control mice, providing direct evidence that H. pylori infection stimulated the activation of STAT3 in the stomach. By comparing the gene expression profiles, we identified a total of 849 aberrant expression genes enriched in 11 cancer pathways in H. pylori induced STAT3 activation in gastric cancer cells. We further identified 6 candidates (BRUNOL4, FGFR1, SHOX2, JAK3, MAPK8, and PDPN) were directly up-regulated by H. pylori induced STAT3 activation.

Conclusions: H. pylori infection triggers the activation of STAT3 and de-regulates multitude of tumorigenic genes which may contribute to the initiation and progression of gastric cancer.

Ref. No.: 10090942

P114-Ab0133
Role of Toll-like Receptors in Naturally Occurring Influenza

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Background: We investigated the roles of Toll-like receptors (TLRs) in naturally occurring influenza.

Methods: A prospective, case-control study was conducted. Adults hospitalized with virologically confirmed influenza A infections (onset <48 hours, before treatment) were compared with age-/gender-matched controls. TLRs (2, 3, 4, 7, 8, 9) expression in monocytes and dendritic cells (DCs - total, myeloid, plasmacytoid) was quantitated using flow cytometry. Gene expression of RLRs (RIG-1, MDA-5) was evaluated using real-time PCR. Concomitant signaling molecules expression, plasma cytokine/chemokine concentrations, and respiratory tract viral loads were measured. PBMCs were cultured and stimulated ex vivo with TLR-specific ligands for cytokine responses.

Results: Forty two patients with influenza (24 A/H3N2, 18 A/H1N1pdm09) and 20 controls were studied. Patients' mean age was 68 16 years; 81% had respiratory/cardiovascular complications. There were increased cellular expressions of TLR9, TLR8, TLR3, and TLR7 during influenza; TLR2 and TLR4 were suppressed. Results were similar for both virus strains. Higher TLR expression levels at presentation significantly correlated with lower viral loads (Spearman's rho: 046 to 069 for TLR9, TLR8, and TLR3; P-values <005). Multivariate regression models (adjusted for age, comorbidity, disease severity, time from onset) confirmed their independent associations. Increased signaling molecules (phospho-MAPKs, IkB) and inflammatory cytokines (IL-6, sTNFR-1, CCL2/MCP-1; CXCL10/IP-10, IFN-c) correlated with increased TLR expression. RLRs were upregulated simultaneously. PBMCs of patients with influenza showed significant, dynamic changes in their cytokine responses upon TLR stimulation, compared with controls.

Conclusions: Our results suggest that TLRs play an important role in early, innate viral inhibition in naturally occurring influenza. Inflammatory cytokine responses are concomitantly induced. These findings support investigation of TLR targeting as a novel intervention approach for prophylaxis against influenza.

Ref. No.: 09080102

P115-Ab0101
Prevention and Treatment of Swine Origin Influenza Virus (S-OIV) through the Use of Interferon: An in vivo and ex vivo Study

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Background: H1N1pdm infection emerged in 2009 as the first influenza pandemic of the 21st century and originated from a swine precursor virus. Though this new virus was associated with a low mortality compared with seasonal influenza and with another new emerging influenza virus (H5N1), the main concerns that exist were the mortality in younger patients (contrasting with a bias towards elderly patients with seasonal influenza) and the potential for this virus to re-assort with avian influenza viruses resulting in a highly transmissible virus with a high mortality.

Objectives: To determine if prophylactic and/or therapeutic administered interferon alpha to ex vivo bronchial and lung tissues would be able to reduce H1N1pdm influenza infection.

Methods: Fresh bronchial and lung tissues were obtained from patients undergoing elective surgery with lobectomy. They were cultured with and without interferon and then infected with H1N1pdm virus. After 24 and 48 hours incubation the quantity of virus produced and the cellular genes involved in the antiviral response were analyzed by PCR and by SuperArray.

Results: Prophylactic interferon was able to reduce infection with H1N1pdm in lung tissues. Therapeutic interferon was beneficial in lung tissues but not in bronchial tissues.

Conclusions: Exogenous interferon will be useful for pulmonary involvement of influenza viruses (H1N1 and H5N1) but may not be of significant benefit for bronchial infection.

Implications: For influenza virus infections that are resistant to currently available antiviral agents, interferon therapy offers a potential benefit. This therapy has recently been used in a macaque model of H5N1 infection resulting in a decrease in the

alveolar inflammatory response.

Ref. No.: 10090202

P116-Ab0102
Profiling of Substrate-Specificity and Rational Design of Broad-Spectrum Peptidomimetic Inhibitors for the 3C-Like Proteases of Coronaviruses

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Coronaviruses (CoV) are associated with up to 5% of respiratory diseases. There are three groups of CoV, namely alphacoronavirus (group 1), betacoronavirus (group 2), and gammacoronavirus (group 3). Replication of CoV requires an active 3C-like protease that processes the viral polyprotein into mature functional proteins. Supported by a HMRF grant, our group has profiled the substrate specificity of the 3C-like proteases from human CoV NL63 (group 1), human CoV OC43 (group 2a), SARS-CoV (group 2b), and infectious bronchitis virus (IBV; group 3). Based on the substrate specificity profile obtained, we have designed a 'super-active' substrate with ~2-3 fold increase in cleavage efficiency. We also designed a number of nitrile-based peptidomimetic inhibitors and test their inhibitory effects on the 3C-like proteases. The best inhibitor, Cbz-AVLQ-CN, was able to inhibit 3C-like proteases from a broad spectrum of coronaviruses (human CoV 229E, NL63, OC43, HKU1, SARS, and IBV) with IC_{50} values of 1.3 – 3.7 mM. Our work provides invaluable insights into the design of drugs to combat future outbreak of coronavirus infections.

Ref. No.: 09080282

P117-Ab0103
Molecular Epidemiological Investigation of PARV4-related Viruses in Hong Kong and Southern China

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Introduction: Many emerging infectious diseases are zoonoses that cause epidemics in humans after overcoming the inter-species barrier. Identifying possible animal origins or counterparts of emerging viruses is important in understanding their epidemiology, evolution and potential for re-emergence. Parvoviruses are widespread pathogens that cause a wide range of disease in animals. Human parvovirus 4 (PARV4) was identified in 2005, but the epidemiology, mode of transmission, clinical significance and origin of this newly identified virus are still poorly understood. In particular, unlike the other human parvoviruses with related viruses in animals, PARV4 was phylogenetically distinct without closely related animal counterparts.

Methods: To identify possible animal origins of PARV4 or related viruses, a surveillance study for PARV4-like viruses in human and animal samples was conducted. Nearly full-length sequences of the identified PARV4-related viruses from sheep, swine, cattle and human were determined and analyzed.

Results: PARV4-like viruses were detected by PCR among 44.4% (148/333) of porcine samples (including lymph nodes, liver, serum, nasopharyngeal and fecal samples), 13% (4/32) of

bovine spleen samples, 1.8% (2/110) of bovine liver samples, 71.4% (10/14) of ovine spleen samples, 66.7% (6/9) of ovine liver samples and 2% (7/362) of human serum samples sent for HIV and HCV antibody tests. Four distinct parvoviruses were identified, including three novel parvoviruses, ovine hokovirus (OHoV), porcine hokovirus (PHoV) and bovine hokovirus (BHoV), and PARV4 from humans. Analysis of genome sequences from four OHoV, seven PHoV, five BHoV and one PARV4 strains showed that the animal parvoviruses were most similar to PARV4 and together formed a distinct cluster within Parvoviridae. The four parvoviruses also differed from other parvoviruses by their relatively large predicted VP1 protein and the presence of a small unique conserved putative protein. Based on these results, we propose a separate genus, Hokovirus, to describe these three parvoviruses. The co-detection of porcine reproductive and respiratory syndrome virus, the agent associated with the recent "high fever" disease outbreaks in pigs in China, from our porcine samples warrants further investigations.

Discussion and Conclusions: Three novel parvoviruses, OHoV, PHoV and BHoV, were discovered in Hong Kong. Animal viruses closely related to PARV-4 were identified in porcine and bovine samples, suggesting that interspecies transmission could have occurred during their evolution. This has dramatically improved the understanding of the origin of PARV-4 and this group of novel viruses. Since these animals are common food animals, further studies are warranted in studying the pathogenesis and epidemiology of these novel parvoviruses.

Ref. No.: 08070712

P118-Ab0105
Anti-ganglioside Antibodies were not Detected in Human Subjects or Mice Infected with or Vaccinated Against 2009 Pandemic Influenza A (H1N1) Virus

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Background: Mass vaccination against influenza A virus (H1N1) was terminated in USA in 1976 due to significantly increased risk of Guillain-Barré syndrome (GBS), an acute, immune-mediated demyelinating disorder that can cause paralysis and death. Anti-ganglioside antibodies underlying the development of GBS were reported by another group to be induced in mice receiving an H1N1 vaccine produced in 1976, another vaccine against influenza, or influenza hemaggulutin (HA).

Objectives: The overall goals of this pilot study are to verify the ability of swine-origin H1N1 influenza virus HA to induce anti-ganglioside antibodies in mice and if possible to map the peptide sequence associated with this induction. Because human subjects infected with or vaccinated against pandemic H1N1 2009 (pdm09) were available after the submission and approval of our proposal, we also expand our study to analyze anti-ganglioside antibodies in individuals infected with or vaccinated against pdm09, including eight confirmed cases of post-vaccination GBS.

Methods: PANFLU.1 vaccine against pdm09 in Freund complete adjuvant was used to immunize C57 mice. Serum samples from infected or vaccinated human subjects or mice were collected. Antibodies against GM1 and other gangliosides were detected by commercial ELISA kits. HAI titers in serum samples were also analyzed.

Results: Neither anti-GM1 antibodies nor any other anti-ganglioside antibodies were detected in any human subject tested or in vaccinated mice.

Conclusions: Our results did not support the induction of anti-ganglioside antibodies by influenza viruses or vaccines.

Implications: Our findings overturn previous notion in the field and correct the literature. They have now been independently verified by a leading group in the field. Our work has important implications in the prevention and management of severe side effects associated with influenza vaccination.

Ref. No.: 10091432

P119-Ab0106
Influenza A Virus NS1 Protein Suppresses Innate Antiviral Response by Targeting Double Stranded RNA-binding Protein PACT

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Introduction: Influenza A virus (IAV) is a common human pathogen causing devastating pandemics and seasonal epidemics. Innate antiviral immune response exemplified by the production of type I interferons (IFNs) is induced when IAV is recognized by Toll-like receptors and RIG-I-like receptors. To counteract and ensure its successful replication and infection, IAV encodes IFN-antagonizing non-structural protein NS1, a multi-functional double-stranded RNA binding protein that interacts with both retinoic acid-inducible gene I (RIG-I) and protein kinase R (PKR) to circumvent host antiviral defense.

RIG-I is a cytosolic sensor of IAV. It senses short double-stranded RNA (dsRNA) with 5' triphosphate end which is formed during viral genome replication. We have previously shown that RIG-I requires PACT for full activity. PACT is a cellular dsRNA-binding protein originally identified to be an activator of PKR. How IAV NS1 might affect the function of PACT in innate antiviral response remains to be understood.

Results: We demonstrated that NS1 physically interacts with PACT to perturb RIG-I-dependent IFN production. We also characterized the role of PACT in NS1-mediated suppression of RIG-I-induced IFN response. PACT is a novel target of IAV IFN-antagonizing protein NS1. PACT-mediated potentiation of RIG-I activation on IFN-ß reporter activity was significantly inhibited by NS1. PACT also acts as an inhibitor of IAV polymerase transcriptional activity. By RNA-nucleoprotein complex (RNP) reconstitution assay, it was shown that overexpression of PACT could significantly dampen the RNP activity. The observed PACT-mediated suppression of RNP activity could be partially rescued by overexpression of NS1 protein. This suggests the counteracting roles of PACT and NS1 during IAV infection. The inhibitory role of PACT during IAV infection is further supported by our observation that knockdown of PACT in cells promoted IAV replication. Furthermore, we demonstrated IFN dependence of PACT-mediated suppression of RNP activity which helps to understand the underlying mechanism for PACT function. Finally, strain difference in the suppression of PACT by IAV NS1 protein was also documented.

Significance and Implications: Our findings not only suggest a novel and crucial role for influenza NS1 protein in targeting PACT to evade host immune response but also provide new insights into the inhibitory mechanism of PACT on IAV replication and infection. NS1-deleted IAVs have been tested as vaccines. Peptide mimetics and small molecule agonists of PACT might be used as adjuvants and anti-influenza agents. Thus, our work also reveals new strategies for development of vaccines and anti-influenza drugs.

Ref. No.: HK-09-02-06

P120-Ab0108
Preparedness and Responses of At-Risk Groups (frontline healthcare workers in community clinics, community outreach teams and elderly homes) to Pandemic Influenza in Hong Kong

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Background: Preparing for health threats is particular important for community doctors as they are the first point of contact for patients entering a healthcare system.

Methods: Quantitative and qualitative studies were conducted to study healthcare workers responses to deal with pandemic influenza. Three cross-sectional surveys were conducted among 1) registered doctors in Hong Kong; 2) doctors who worked in public primary care clinics 3) community nurses. For qualitative studies, 70 interviews on 1) healthcare workers from isolation ward; 2) designated fever clinic and 3) elderly home were conducted with the content of interviews audio-taped and transcribed verbatim.

Results: For the cross-sectional survey on doctors and nurses, we showed that there was an increased workload (25% of doctors in cross-sectional survey, 59% of GOPC doctors and 36% of CNS nurses) as a result of H1N1 influenza. We also found that self-reported hand-washing between and after patient contact was less frequently practiced as compared to mask wearing as preventive measures for dealing with influenza H1N1 among doctors (all registered doctors: 53% vs. 78% and GOPC doctors: 54% vs. 99% for washing hands and wearing masks in the past 3 days respectively) although this difference was not observed among CNS nurses. Moreover, although public doctors were more likely to use guideline in dealing with H1N1 influenza, both doctors (all registered doctors: 45%, GOPC doctors: 65%) and nurses (75%) felt that more education and training in dealing with influenza H1N1 was needed. There was a lower willingness to accept H1N1 influenza vaccination among community nurses (73%) when compared to doctors (all registered doctors: 50% and GOPC doctors: 56%). Qualitative studies confirmed that there was increased stress and workload during the pandemic and that frequent change of policy and perhaps lack of education on influenza vaccination could contribute to increased stress among healthcare workers.

Conclusions: We found that there was an increased in clinical service demand for doctors and nurses alike especially those who worked in public facilities. We also showed that the compliance to washing hands were lower among doctors as compared to the wearing of masks and that there was a lower willingness to accept H1N1 influenza vaccination among CNS nurses. Since hand hygiene and influenza vaccination are effective methods

to prevent the spread of influenza infection, future studies can explore reasons for the non-compliance of these preventive behaviors among doctors and nurses.

Ref. No.: CU-09-01-06

P121-Ab0110
Natural Killer Cell Activity Against Human Swine Influenza Viruses

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Introduction: Influenza A (fluA) virus is one of the major causative pathogens of acute respiratory diseases with substantial annual morbidity and mortality worldwide. The potential for the emergence of the new pandemic strains through virus genetic reassortment to which the human population is immunologically naive remains the major concern for public health. Even in the absence of prior immunological memory, host innate immune responses play critical roles in host defense against influenza viruses by limiting viral replication and helping initiate adaptive immune response during the early phase of viral infection. Natural killer (NK) cells, as the key effector cells in the host innate immune system, play a critical role in the first line of host defense against acute viral infections. Recently we and others found that seasonal H1N1 fluA virus can evade NK cell immunity. However, whether swine origin H1N1 fluA virus (pandemic H1N1) has similar immunoevasion to NK cells are still unknown.

Aims: To determine whether human swine influenza virus (pandemic H1N1) can directly infect human NK cells, induce their apoptosis, and reduce NK cell activity.

Methods: Human NK cells were purified from peripheral blood mononuclear cells with NK cell isolation kit. The apoptosis of virus-treated NK cells will be measured by PI staining and analyzed by flow cytometry. The cytotoxic activity of NK cells against target cells was determined by LIVE/DEAD cell-mediated cytotoxicity kit.

Results: Using immunofluorescent microscopy and flow cytometry, we found that pandemic H1N1 virus directly infected human NK cells. Furthermore, pandemic H1N1 virus induced NK cell apoptosis as evidenced by the increased PI+ NK cells after virus infection, as compared to the mock-treated NK cells. Using K562 cells as the target cells, we found that pandemic H1N1 virus treated-NK cells had a significantly lower cytotoxic activity than mock treated-NK cells.

Conclusions: These results demonstrated that the newly-emerged swine fluA H1N1 virus could directly infect NK cells, induce NK cell apoptosis and further reducing NK cell activity. Our results indicated that swine fluA H1N1 virus has also developed a strategy to evade NK cell-mediated innate immunity by which is likely to facilitate viral transmission and may also contribute to virus pathogenesis.

Ref. No.: HK-09-03-05

P122-Ab0111
Comparative Study of Human Papillomavirus (HPV) Prevalence in Homosexual and Heterosexual Male Population in Hong Kong

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Background: Human papillomavirus (HPV) infection causes cervical cancer and anogenital warts. HPV was also found to be associated to various cancers including cancer of anus, penis, oropharynx and esophagus in both men and women. Therefore, HPV infection is a significant problem in both genders. HPV infection has been found to be common in male populations worldwide. The HPV prevalence in genital area of men was 50% (a study in Americas investigating 1159 men from USA, Brazil and Mexico). Risk factors of HPV infection in men include number of life time and current sexual partners, circumcision, condom use and education. There is no study in Asian populations on the prevalence, genotype distribution profile or associated risk factors of HPV infection in male population.

Objectives: This project is to study and compare the prevalence of HPV in men having sex with men (MSM) and men having sex with women (MSW) and to identify their associated epidemiological factors in Hong Kong.

Methods: Male subjects aged 18 to 50 were recruited from Family Planning Association and the Voluntary Counseling and Testing program for HIV and Syphilis organized by AIDS Concern. A self-administered questionnaire was used for assessing the associated epidemiological factors. Swabs from oral, genital and peri-anal were taken from patients for HPV test. Logistic regression was used to identify the independent risk factors of HPV infection.

Results: Total of 208 heterosexual and 209 homosexual men were recruited. The overall HPV prevalence in the MSW and MSM were 21.2% and 28.2%. The HPV prevalence detected in oral region was the same in both groups (4.3% vs. 4.3%). The HPV prevalence detected in peri-anal region were 7.8% and 31.8% for MSW and MSM. In penile region, the HPV prevalence was 17.2% and 10.3% in MSW and MSM. HPV 11, HPV16, HPV 18 and HPV 45 were most commonly detected in MSW. HPV 6 and HPV 11 were most common in MSM. Use of condoms demonstrated protection in HPV infection in genital region in MSW. The number of lifetime sexual partners and having non-regular sexual partners were associated with risk of HPV infection in perianal and genital region in MSM.

Conclusions: HPV prevalence of male population (both MSW and MSM) in Hong Kong is relatively lower than the figures reported in western countries. Further studies are warranted to investigate the natural history of HPV infection in men so as to provide targeted education and prevention strategy.

Ref. No.: CU-10-04-01

P123-Ab0112
Wound Microbiology among Chronic Wounds in Primary Care

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Introduction: Wound care is one of the most time-consuming tasks for primary care nurses. In Hong Kong, our 74 public primary

care clinics manage an estimated one million dressings annually. Effective wound management under the setting of such a high patient volume requires accurate and up to date information on pathogen epidemiology as well as antibiotic resistance patterns.

Aims: To generate epidemiological data on pathogen prevalence and antibiotic resistance among non-surgical chronic wounds in Hong Kong's primary care.

Methods: Wound swabs from consecutive consenting patients presenting to public primary care clinics with non-surgical wounds from October 2011 to August 2013 were sent to the university hospital microbiology laboratory within 24 hours for culture and sensitivity analysis.

Results: Among the 150 patients recruited, 60% received an antibiotic in the previous year. The culture of 61% of wounds considered to be infected on clinical grounds grew pathogenic organisms. MRSA was isolated in 3.6%. Previous antibiotic use (OR 1.2, 95% CI 1.03-1.40), peri-wound skin remaining intact (OR 0.27 95% CI 0.10-0.71) and underlying diabetes (OR 2.43 95% CI 1.15-5.12) were factors that significantly contribute to antibiotic resistance. Factors that contribute to a positive wound culture include underlying diabetes (OR 2.82 95% CI 1.22-6.52) and moderate/large amount of exudate (OR 3.19 95% CI 1.32-7.71).

Conclusions: A large proportion of primary care wounds have a positive culture, but only all isolate pathogenic organisms. The constellation of signs and symptoms for clinical infection did not predict a positive culture, and clinicians/nurses can consider results from this study to guide their future clinical practice.

Ref. No.: CU-10-03-02

P124-Ab0116
Toward a Bioshield against Influenza Virus Infection by Commensal Bacteria Secreting Antiviral Peptide

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Avian influenza (AI) was probably first described in 1878, and it has been found around the world in many countries such as UK and China. In 1997, the avian influenza viruses (AIV) were found to cross the species barrier to infect human beings and cause respiratory illness and deaths in Hong Kong. H5N1 viruses have later re-emerged in Asia with human infections. More than 50% of the human infections were fatal. This raised concerns over an imminent influenza pandemic. The objective of this project is to genetically engineer naturally occurring bacteria to provide protection against influenza A virus by secreting peptide that interfere with viral attachment, and provide a natural bioshield for the protection against influenza A virus by introducing and colonizing these genetically modified bacteria in the oral mucosa and respiratory track of uninfected individuals. The results will be discussed in our presentation.

Ref. No.: 08070592

P125-Ab0119
Prevalence of Carriage and Characterization of MRSA in Slaughter Pigs and Personnel Exposed to Pig Carcasses

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Background: Methicillin-resistant Staphylococcus aureus remains a significant human pathogen. Reports from Europe and North America have documented MRSA colonization of pigs and contamination of pig farmers. Pigs have been implicated as the source of MRSA infections in humans. We determined the prevalence of porcine MRSA colonization in pigs and pig handlers in Hong Kong.

Objectives: To investigate prevalence of MRSA-colonization of (a) pig carcasses from Hong Kong wet markets and (b) live pigs at farms in Hong Kong and China. To determine prevalence of MRSA in workers occupationally exposed to pigs. To determine antibiotic susceptibility and molecular characteristics of strains and to compare with porcine strain ST398 from Europe.

Methods: Nasal swabs collected from: 400 pig carcasses (Hong Kong markets); 475 live pigs (two pig farms in Hong Kong, two in mainland China); 300 butchers employed at wet markets Hong Kong were cultured on MRSA selective agar. Susceptibility testing was performed on isolates confirmed as S. aureus. MecA presence was confirmed. Isolates were characterized by PFGE (using sma1), SCCmec, spa, and MLST type. Presence of genes for antibiotic susceptibility determinants, staphylococcal enterotoxins, and antiseptic resistance was determined. Butchers completed a questionnaire on risk factors for MRSA carriage.

Results: 39% of pig carcasses were MRSA-colonised. All isolates were SCCmec Type IV (92%) or V (8%) and belonged to spa type t899 (ST9) or closely related variants. There was a high level of multi-drug resistance but no resistance to linezolid or tigecycline. Resistance to vancomycin was observed in 16 carcass isolates. 5.7% of butchers were colonized, the predominant strain also being ST9. No live pigs in Hong Kong yielded MRSA but a high percentage of pigs in both mainland farms were colonised (48% Farm 1; 39% Farm 2). All isolates were negative for the multi-drug resistance gene cfr. No virulence factors were detected.

Conclusions: There was a high rate of colonisation of slaughtered pigs with multi-drug resistant MRSA ST9. This was also the predominant strain colonising butchers and appears to be the main porcine strain in Asia. The presence of MRSA in live pigs from China suggests widespread colonisation in the mainland.

Implications: Pigs may represent an important reservoir of MRSA. Personnel occupationally exposed to pigs/pig carcasses can become colonised which can increase the risk of infection with this multi-resistant strain.

Ref. No.: 08070912

P126-Ab0122
Investigating the Effects of Minocycline as Neuroprotective Agent against Cytokine Storm-Mediated Neurotoxicity

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Introduction and Aims: In Hong Kong, a high percentage (20%) of influenza patients, mostly children, are suffering from neurological complications after recovery from the infection. During influenza infection, the increase in systemic cytokine

levels leading to cytokine storm is an important pathogenesis in the patients. Studies have suggested that both systemic and local elevation of cytokine levels could result in cognitive impairment and neurotoxicity. This study aims to investigate if minocycline, a tetracycline, could elicit neuroprotection against neurodegeneration induced by elevated level of cytokines.

Methods: We set up two in vivo models to test the effects of minocycline. In the first model, SD rats were injected with mixed cytokine (TNF-α, IL1-β, IL6, IL8, IFN-α, MCP-1, MIP-1α) to mimic peripheral cytokine storm. In the second model, we also investigated the effects of minocycline against local cytokine storm. In rats with intracerebroventricular (i.c.v.) injection of mixed cytokine. To further study the direct effects of minocycline on neurons, we used an in vitro model in which primary cultured hippocampal neurons were exposed to mixed cytokine.

Results: In the first model, we found that minocycline had anti-inflammatory effects and it suppressed the activation of microglia and astrocytes. In the same time, it restored the level of total tau and phosphorylated tau to a level comparable to the control. However, minocycline treatment alone could also affect the intracellular distribution of tau and the expression of pre synaptic protein synaptophysin. In the second model, the levels of phosphorylated tau and total tau increased in the hippocampus. Minocycline reduced the level of phosphorylated tau but it could not reduce that of total tau. Minocycline also suppressed mixed cytokine-induced activation of astrocyte and microglia. However, minocycline in the same time markedly decreased the expression of presynaptic proteins synapsin-1 and synaptophysin. Similar to the in vivo study, the levels of phosphorylated tau and total tau in cultured hippocampal neurons were increased upon mixed cytokine treatment. Minocycline partly reduced the level of phosphorylated tau but not that of total tau. It also slightly reduced the levels of drebrin in mixed cytokine treatment group.

Conclusions: The results suggested that minocycline was able to restore some of the parameters changed during peripheral and local cytokine storm. However, minocycline itself might also have an impact on synaptic proteins. Further experiment is required to confirm if minocycline is protective or deleterious in neurons stressed by cytokine storm.

Ref. No.: 09080822

P127-Ab0123

A Role of IL-17A in Modulating Intracellular Survival of Mycobacterium bovis BCG in Murine Macrophages

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IL-17A is a crucial immunomodulator in various chronic diseases including rheumatoid arthritis and inflammatory bowel disease. It has also been demonstrated the dysregulation of cytokine and chemokine productions at mycobacterial infection also involved IL-17A. Whether IL-17A regulates innate defense mechanisms in response to mycobacteria infection remains to be elucidated. Our results demonstrated that the pretreatment of RAW264.7 murine macrophages with recombinant IL-17A for twenty-four hours prior to mycobacteria infection suppressed the intracellular survival of Mycobacterium bovis Bacillus Calmette-Guérin (BCG). Since our data showed killing of intracellular mycobacteria could be abolished by nitric oxide (NO) inhibitor, we measured the level of NO and the expression of NO inducer, inducible nitric oxide synthase (iNOS) in IL-17A pretreated BCG-infected RAW264.7 macrophages. We showed that IL-17A pretreatment was able to

synergistically enhance BCG-induced NO production and iNOS expression in dose- and time-dependent manners. In addition, we further delineated the mechanisms involved in this synergistic reaction. IL-17A was found to specifically enhanced BCG-induced phosphorylation of JNK, but not ERK1/2 and p38 MAPK. By using specific JNK inhibitor SP600125, we found that the production of NO in BCG-infected macrophages with IL-17A pretreatment was significantly suppressed. Taken together, we confirmed the involvement of the JNK pathway in IL-17A-enhanced NO production in BCG-infected macrophages and subsequently enhanced the clearance of intracellular BCG by macrophages. In conclusion, our study revealed an anti-mycobacterial role of IL-17A through priming the macrophages to produce NO in response to mycobacteria infection.

Ref. No.: 09080542

P128-Ab0129

Impact of Universal Vaccination with the 7-valent Conjugate Pneumococcal Vaccine (PCV7) in Hong Kong on the Incidence of Pneumonia Hospitalization and Carriage in Children

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Background: Universal childhood PCV immunization was implemented in 2009 in Hong Kong.

Objectives: To document the impact of universal vaccination with PCV on pneumonia hospitalization in Hong Kong children and on the colonization of pneumococcus and S. aureus.

Study Design: Part I comprised a prospective population-based study of pneumonia hospitalization in children < 18 years between 2010-2013; Part II was a longitudinal surveillance of Pneumococcal and S. aureus carriage in the same period.

Methods: Part I: Children < 18 years admitted for acute respiratory tract infection on one fixed day a week to the only 2 public hospitals on Hong Kong Island were recruited. Bacterial pneumonia was diagnosed by independently by radiologists following the WHO CXR Protocol and by paediatricians. A questionnaire captured vaccination history and socioeconomic cost. Part II: A nasal swab and a nasopharyngeal swab were obtained for culture and PCR from all children < 5 years admitted to QMH who consented. A questionnaire captured immunization and relevant history.

Results: The mean annual age-specific rate of bacterial pneumonia after the universal implementation of PCV7 for children < 5 years was 808.2 (95% CI: 569.0, 1114.0) and 521.7(95% CI: 335.9, 780.0) per 100,000 diagnosed by pediatricians and by the WHO CXR Protocol, respectively. Carriage of PCV 7 serotypes drastically decreased while non-PCV serotype 15A rose to 11.8% in 2012/13 (p=0.004). There was no change in the prevalence of MSSA and MRSA carriage.

Conclusions: There was no reduction of bacterial pneumonia hospitalization in children < 5 years after the universal implementation of PCV when compared to the period before the registration of PCV. Carriage of non-vaccine serogroup 15 subtypes has become more prevalent.

Implications: PCV immunization status does not preclude a high index of suspicion for bacterial pneumonia in young children. Continuous monitoring of serotype replacement is needed.

Ref. No.: CHP-CE-06

P129-Ab0130
Infection Control Intervention on Methicillin-resistant Staphylococcus Aureus (MRSA) in Residential Care Homes for the Elderly (RCHEs)

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Background: The frail elderly living in institutions is known to be at high risk for MRSA acquisition. However, no study on the MRSA burden, the mechanisms of MRSA diffusion and the control strategies in local RCHEs are available.

Objectives: To evaluate the effectiveness of a multifaceted infection control intervention bundle in controlling the MRSA transmission in RCHEs.

Methods: This was a cluster randomized controlled trial with an intervention arm and a usual care arm. It started with a baseline assessment, followed by an intervention phase, quarterly assessments and post-intervention follow-ups. RCHEs located in Kowloon central districts with a bed capacity from 50 to 300 were invited. Nasal swabs from consented residents, microbiological cultures for staff hand hygiene (HH) effectiveness and environmental hygiene were evaluated. Direct observations on staff HH compliance were also performed. Intervention bundle focused on HH, environmental hygiene, and modified contact precautions was promulgated to the intervention arm by infection control nurses through lectures, on-site demonstration, and telephone consultation.

Results: A total of 2776 residents from 36 RCHEs joined our study at baseline. The overall MRSA prevalence was 20.4% and the median duration for MRSA clearance was estimated to be 9 months. Inter-facility MRSA transmission rate from hospital to RCHE was 13.3%. A 7.8% decrease in the MRSA prevalence at intervention arm whereas a 4.9% increase at usual care arm was detected, though both were not statistically significant. Staff HH compliance was very low at baseline but increased significantly from 5.9% to 45.6% in the intervention arm at post-intervention. (P<0.001)

Conclusions: We successfully initiated the infection control culture into the RCHEs. However, this behavioural change takes time to emerge. The implementation of the infection control bundle did not translate into a statistically significant MRSA reduction during our study period. The substantial burden through the two-way MRSA transmission channel between RCHEs and hospitals, and the high proportion of long-term and intermittent MRSA shedders might render the intervention effectiveness. Other approaches to bring a sustainable MRSA reduction should be considered.

Ref. No.: CHP-NS-04

P130-Ab0131
Enteric Involvement of Seasonal Influenza A Virus Infection and its Pathogenesis

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Background: Gastrointestinal (GI) symptoms such as diarrhea and vomiting are occasionally reported in seasonal influenza patients.

Objectives: To evaluate the prevalence of seasonal influenza A viruses in stool of adult patients with confirmed influenza A infection and to investigate whether seasonal influenza A viruses infect and replicate productively in human gastrointestinal tract.

Methods: Prospective, observational cohort design with laboratory investigation. Stool specimens were collected from adults hospitalized for seasonal influenza A during a 4-year period (2006-2009) and were tested for viral RNA by probed-based RT-PCR assay. Medical records were reviewed. The virus potential to cause direct GI tract infection was studied through in vitro receptor staining and virus-binding experiments on human small and large intestinal tissues.

Results: Altogether 119 patients were studied. Fecal viral RNA was frequently detected in 56/119 (47%) cases, whereas viable viruses were rarely (3.6%) isolated from stool. Fecal viral RNA detection in these patients had little correlation with GI symptoms and clinical outcomes, but was independently associated with clinical features suggestive of high virus burden, including positive virus isolation from nasopharyngeal-aspirates [adjusted odds ratio, AOR 3.76(95%CI=1.07-13.20), p=0.039] and lymphopenia [AOR 2.36(95%CI=1.02-5.47), p=0.045]. Virus receptor was absent on the intestinal epithelial surface but present in the lamina propria. Both seasonal H1N1 and H3N2 viruses bind to intestinal DC-SIGN$^+$ CD68$^+$ cells.

Conclusions: Lack of clinical correlations with GI symptoms and mechanistic studies suggest that direct GI tract infection by seasonal influenza A viruses is unlikely. Frequent fecal RNA presence may be related to the detection of viral RNA remnants in homed infected intestinal immune cells from "spillover" of high virus burden in severe infections.

Ref. No.: CU-09-01-02

P131-Ab0033
Gene Expression Profiling of CD4$^+$ T Cells in Treatment-naive HIV, HCV Mono- or Co-infected Chinese

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Background: Because of the shared transmission routes, co-infection with human immunodeficiency virus and hepatitis C virus is very common. Accumulated clinical evidence showed that one could alter the infectious course of the other virus in HIV and HCV co-infected individuals. However, little is known on the molecular basis of HIV/HCV interactions and their modulations on hosts.

Methods: In this study, treatment-naive HIV, HCV mono-/co-infected individuals with CD4$^+$ T cell counts >300/μl were recruited and their gene expression profiles were investigated by microarray assays. The differentially expressed genes were identified and validated by quantitative real-time PCR (qRT-PCR). To further understand the biological meanings of the gene expression profiles in these three groups, GSEA analysis (version 2.0, Broad Institute http://www.broad.mit.edu/gsea) was performed.

Results: By gene set enrichment analysis, we revealed that gene sets of cell cycle progression, innate immune response and some transcription factors in CD4$^+$ T cells were mainly affected by HIV;

while genes associated with GPCR signaling were the major targets of HCV. Metabolic pathways were modulated by both HCV and HIV viruses.

Conclusions: This study for the first time offers gene profiling basis for HCV/HIV mono-/co- infections in human beings. HIV infection displayed the great impact on transcription profile of CD4^{+} T cells in HIV/HCV co-infected individuals. Genes related to cell cycle arrest were significantly mediated by HIV which may lead to dysfunction of CD4^{+} T cells and acceleration of HCV-related disease progression in the co-infections.

Ref. No.: 09080482

P132-Ab0100
Susceptibility of the Upper Respiratory Tract to Influenza Virus Infection Following Desialyation

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Background: Influenza infection begins with the attachment of the viral haemagglutinin (HA) to the surface receptor of a cell. This binding involves a glycan called sialic acid (Sia). Previous studies have suggested that the affinity of influenza viruses isolated from different species depends on the linkage between this Sia and the adjacent sugar (usually galactose). In general, human and swine viruses prefer Sia with an α2-6 linkage while avian viruses prefer an α2-3 linkage. Though there are commercially available therapies that block influenza virus release, there has been limited information on controlling influenza virus infection by removing Sia from the host surface.

Objectives: The objectives of this study were firstly to identify the Sia present in the human respiratory tract and then see if these receptors were still present after sialidase treatment. We then investigated whether removal of this Sia by sialidase would reduce influenza infection in ex vivo tissues.

Methods: We used lectin histochemistry to identify the Siaα2-6 and Siaα2-3 linkage and then re-examined this lectin binding after topical sialidase treatment. We then analyzed the tissues for the presence of sialylated glycans using mass spectrometry. Finally we tested the infection of human upper and lower respiratory tract tissues after sialidase treatment with avian and human viruses.

Results: We found that there was a diffuse expression of Siaα2-6 throughout the upper and lower respiratory tract. Siaα2-3 varied according to site with more N-linked Siaα2-3 glycans in the upper respiratory tract and more O-linked glycans in the lower respiratory tract. Sialidase treatment was able to remove both types of glycans. Unexpectedly we found that the effect of desialylation was not the same in all cell lines tested.

Conclusions: We found that both prophylactic as well as therapeutic sialidase treatment was able to prevent infection with avian and human influenza viruses and that the ex vivo model was a useful study tool for testing the efficicacy of novel therapeutic agents.

Implications: Sialidase therapy offers a potentially useful clinical option and this has now being used in a Phase II clinical trial for influenza and another sialic-acid receptor based infection caused by parainfluenza viruses.

Ref. No.: 08070842

P133-Ab0042
Analysis of Influenza Vaccination Policies Before, During and After the 2009 H1N1 Pandemic

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Background: Vaccination is generally considered to be the best primary prevention measure against influenza virus infection. Many countries encourage specific target groups of people to undertake vaccination, often with financial subsidies or a priority list. To understand differential patterns of national target groups for influenza vaccination before, during and after the 2009 influenza pandemic, we reviewed and analyzed the country-specific policies in the corresponding time periods.

Methods: Information on prioritized groups targeted to receive seasonal and pandemic influenza vaccines was derived from a multi-step internet search of official health department websites, press releases, media sources and academic journal articles. We assessed the frequency and consistency of targeting 20 different groups within populations which are associated with age, underlying medical conditions, role or occupations among different countries and vaccines. Information on subsidies provided to specific target groups was also extracted.

Results: We analyzed target groups for 33 (seasonal 2009 and 2009-10 vaccines), 72 (monovalent pandemic 2009-10 vaccine) and 34 (seasonal 2010 and 2010-11 vaccines) countries. In 2009-10, the elderly, those with chronic illness and health care workers were common targets for the seasonal vaccine. Comparatively, the elderly, care home residents and workers, animal contacts and close contacts were less frequently targeted to receive the pandemic vaccine. Pregnant women, obese persons, essential community workers and health care workers, however, were more commonly targeted. After the pandemic, pregnant women, obese persons, health care and care home workers, and close contacts were more commonly targeted to receive the seasonal vaccine compared to 2009-10, showing continued influence from the pandemic. Many of the countries provided free vaccines, partial subsidies, reimbursements or national health insurance coverage to specific target groups and over one-third of the countries offered universal subsidy regarding the pandemic vaccine. There was also some inconsistency between countries in target groups.

Conclusions: Differences in target groups between countries may reflect variable objectives as well as uncertainties regarding the transmission dynamics, severity and age-specific immunity against influenza viruses before and after vaccination. Clarification on these points is essential to elucidate optimal and object-oriented vaccination strategies.

Ref. No.: HK-11-04-03

P134-Ab0004
Aerosol Dispersion During Common Respiratory Therapies: A Risk Assessment Model of Nosocomial Infection to Healthcare Workers

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Introduction, Aims and Objectives: The exhaled air dispersion

distances during application of various respiratory therapies for respiratory failure are unknown. In this infection control study, we examined the exhaled air dispersion distances and directions during application of different respiratory therapies attached to a Human-Patient-Simulator (HPS) in an isolation room with pressure of -5Pa.

Methods: The HPS was positioned at 45° on the bed and programmed to mimic different severity of lung injury. Airflow was marked with intrapulmonary smoke for visualization. A leakage jet plume was revealed by a laser light-sheet and images captured by high definition video. Normalized exhaled air concentration in the plume was estimated from the light scattered by the smoke particles. Significant exposure was defined as where there was ≥20% of normalized smoke concentration.

Results: Significant exposure to exhaled air occurs within 1m from patients receiving non-invasive ventilation via the ComfortFull 2 mask and the Image 3 mask connected to the whisper swivel exhalation port, with far more extensive leakage and room contamination via the latter device, especially at higher inspiratory pressures. The maximum exhaled air distances from application of jet nebulizer and oxygen via nasal cannula, Venturi mask, and the non-rebreathing mask were about 0.8m, 0.42m, 0.4m and < 0.1m respectively.

Conclusions: Healthcare workers should take adequate precautions when providing respiratory support to patients with pneumonia of unknown aetiology complicated by respiratory failure.

Implications:
• It is advisable to choose facemasks with predictable exhaled air directions and distances for non-invasive ventilation.
• It is important to avoid high inspiratory pressures during non-invasive ventilation and the use of whisper swivel exhalation device, which could lead to wider distribution of exhaled air and substantial room contamination.
• More extensive exhaled air dispersion and room contamination occurs during application of a jet nebulizer to patients with more severe lung injury. It is advisable to seek alternative modes for delivery of bronchodilators (eg meter-dose inhaler via an aerochamber or a spacer).

Ref. No.: 06060202

P135-Ab0019

Streptococcus Pneumoniae Carriage in Young Children Shortly after the Universal Use of the 7-Valent Conjugate Pneumocccal Vaccine in Hong Kong

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Introduction: Streptococcus pneumoniae is a major cause of childhood infections. In western countries, the introduction of the 7-valent pneumococcal conjugate vaccine (PCV-7) has led to drastic decline in the incidence of invasive pneumococcal disease caused by serotypes included in the vaccine. The vaccine also protects against carriage of those serotypes in the vaccinated children. In Asia, Hong Kong is one of the first cities to introduce PCV7 into the childhood immunization program and this was implemented since September 2009.

Objectives: To assess the changes in serotype distribution and antibiotic resistance of nasopharyngeal isolates prior to and during the early introduction of PCV7 in Hong Kong.

Methods: Nasopharyngeal specimens were collected from children aged ≤5 years who attend day care centers (DCC) or kindergartens (KG) in Hong Kong during September 2009 to April 2010 (period 2). The finding was compared to a similarly designed study conducted during December 1999 and June 2000 (period 1).

Results: Nasopharyngeal specimens were collected from 1978 and 2221 children attending day care centers or kindergartens in period 1 (1999-2000) and period 2 (2009-2010), respectively. Carriage of PCV7 serotypes decreased from 12.8% to 8.6% (P<0.01). The relative contribution of PCV7 serotypes 14 and 18C had decreased while that for non-PCV7 serotypes 19A, 6A, 6C, 23A and 15B had increased. In period 2, PCV7 penetration rate (at least one dose) for children aged 2, 3, 4 and 5 years were 43%, 35.7%, 26.7% and 20.4%, respectively. In multivariate analysis, PCV7 use was the only independent variable associated with fewer PCV7 serotypes carriage (OR 0.5, P=0.001). In period 2, high rates of dual penicillin/erythromycin nonsusceptibility were found in serotypes 6B (77.3%), 14 (100%), 19F (100%), 23F (78%), 19A (75%), 6A (87.8%), 6C (59.3%) and 23A (78.9%).

Conclusions: In conclusion, this study showed that the proportion of several serotypes among pneumococci carried by children in Hong Kong have changed following the availability of PCV7 and to a lesser extent, PCV10 as self-financed items. Despite some favorable reduction in the vaccine-related serotypes, there was little change in the carriage of antimicrobial-resistant pneumococci and the rates of penicillin and erythromycin resistance among the carried isolates have even increased.

Ref. No.: CHP-CE-08

P35-Ab0055
Modelling the Potential Impact of HPV Vaccination on Hong Kong's Cervical Cancer Burden

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Background: There were around 400 cervical cancer cases diagnosed in Hong Kong annually in recent years. Whereas Hong Kong has introduced an organized cervical screening program since 2004, cervical screening in Hong Kong currently has not yet reached the targeted coverage. For further preventing cervical cancer incidence, the newly developed HPV vaccines which protect against HPV-16/18 infection have been used on top of cervical screening in many developed overseas countries. Therefore, organized HPV vaccination for female adolescents has the potential to significantly reduce cervical cancer burden in Hong Kong.

Methods: We built mathematical transmission models for evaluating the impacts of various female adolescent vaccination strategies on HPV prevalence and cervical cancer incidence in addition to status quo cervical screening in Hong Kong. We analyzed the cost-effectiveness of organized HPV vaccination programs under a societal perspective with annual discount rate at 3% on both costs and quality-adjusted life-years (QALYs). We further performed sensitivity analysis on natural history parameters, costs and health utilities. In the analysis, we considered 1 GDP per capita (US$33,218/QALY) as the incremental cost-effectiveness ratio (ICER) threshold.

Results: Our results suggested that cervical cancer incidence would start decreasing after 30 years the vaccination programs have commenced. The results also suggested that routine vaccination programs among female adolescents were very likely to be cost-effective in reducing cervical cancer incidence when HPV vaccines protected vaccinees for 30 years or more. If vaccine-induced protection lasted for 15 years only, 1-dose boosting could be a strategy to improve the cost-effectiveness of organized female adolescent HPV vaccination programs.

Conclusions: Higher vaccination coverage promoted greater public health impact on reducing HPV prevalence and cervical cancer incidence. However, without an organized vaccination program HPV vaccine uptake in Hong Kong could be low. As such, policymakers should devise well-designed, efficient strategies to attain high vaccination coverage among female adolescents for maximizing the potential population-wide benefit of HPV vaccination.

Ref. No.: CHP-CE-05

P36-Ab0014
Effectiveness of Incorporating Tai Chi in a Pulmonary Rehabilitation Program for Chronic Obstructive Pulmonary Disease (COPD) Patients in Primary Health Care

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Introduction: Studies have shown that pulmonary rehabilitation and Tai Chi are beneficial to patients with Chronic Obstructive Pulmonary Disease (COPD), which is a major public health problem. The aim of this single-blind randomized controlled study was to compare the self-efficacy and quality of life parameters of COPD patients who underwent pulmonary rehabilitation with or without Tai Chi elements incorporated in the exercise component.

Methods: 192 COPD patients, recruited from four primary care clinics, satisfied the eligibility criteria and consented to randomization to either pulmonary rehabilitation program group (PRP) or the group with Tai Chi elements added to PRP (TC). Both groups received rehabilitation consisting of 2 sessions per week for 6 weeks with totally identical content except that Tai Chi exercises were added to TC group. Data collection was performed at baseline, 2 and 6-month post-intervention.

Results: Intention-to-treat analysis was performed for 192 subjects. Both groups did not differ in demographics and baseline variables except for COPD staging, mean FEV1, FEV1%-Pred, Saint George Respiratory Questionnaire SGRQ activity score and COPD-CSES self-efficacy score. Statistical improvements were seen in exercise capacity, health status and self-efficacy within both groups at 6-month post-intervention. Although more favorable improvements in physiological outcomes and health status were demonstrated in Tai Chi group, only the functional exercise capacity showed statistical improvement between groups at 6 months post-intervention (β = 12.786 m; 95% CI = 3.794, 21.777; p = 0.006).

Conclusion: The adjuvant effect of incorporating Tai Chi in pulmonary rehabilitation showed a modest complementary benefit in exercise capacity.

Knowledge Gains and Impact on Health Policy and Practice: As studies including Cochrane review have noted the importance of adherence to exercise prescription maintenance in decreasing the longitudinal decline of benefits after pulmonary rehabilitation, the high compliance rate to Tai Chi after pulmonary rehabilitation are attributing factors leading to more favorable outcomes in the Tai Chi group. The incorporation of Sun Style Tai Chi, which is suitable for older people involving less difficult movement, offers an alternative form of appropriate exercise for COPD patients after pulmonary rehabilitation.

Ref. No.: 08091291

P37-Ab0137
A Multicentre, Prospective, Randomised Controlled Trial to Compare the Pressurized Irrigation Method with Conventional Practice of Swabbing in Cleansing Wounds Healed by Secondary Intention

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Background: Wound cleansing should create an optimal healing environment by removing excess debris, exudates, foreign and necrotic material which are commonly present in the wounds that heal by secondary intention. At present, there is no research evidence for whether pressurised irrigation has better wound healing outcomes compared with conventional swabbing practice in cleansing wound.

Objectives: This study investigated the differences between pressurised irrigation and swabbing method in cleansing wounds that healed by secondary intention in relation to wound healing outcomes and cost-effectiveness.

Design: Multicenter, prospective, randomised controlled trial

Setting: The study took place in four General Outpatient Clinics in Hong Kong

Methods: Two hundred and fifty-six patients with wounds healing by secondary intention were randomly assigned by having a staff independent of the study opening a serially numbered, opaque and sealed envelope to either pressurized irrigation (n=122) or swabbing (n=134). Staff undertaking study-related assessments were blinded to treatment assignment. Patients' wounds were followed up for 6 weeks or earlier if wounds had healed to determine wound healing, infection, symptoms, satisfaction, and cost effectiveness. The primary outcome was time-to-wound healing. Patients were analysed according to their treatment allocation. This trial is registered with ClinicalTrials.gov, number NCT01885273.

Results: Intention-to-treat analysis showed that pressurised irrigation group was associated with a shorter median time-to-wound healing than swabbing group [9.0 days (95% CI: 7.4-13.8) vs. 12.0 (95% CI: 10.2-13.8); p=0.007). Pressurised irrigation group has significantly more patients experiencing lower grade of pain during wound cleansing (93.4% vs. 84.2%; p=0.02), and significantly higher median satisfaction with either comfort or cleansing method (MD 1 [95% CI 5-6]; p=0.002; MD 1 [95% CI 5-6]; p<0.001) than did swabbing group. Wound infection was reported in 4 (3.3%) patients in pressurised irrigation group and in 7 (5.2%) patients in swabbing group (p=0.44). Cost-effectiveness analysis indicated that pressurised irrigation in comparison with swabbing saved per patient HK$ 110 (95% CI -33 to 308) and was a cost-effective cleansing method at no extra direct medical cost with a probability of 90%.

Conclusions: This is the first randomised controlled trial to compare the pressurised irrigation and swabbing. Pressurised irrigation is more cost-effective than swabbing in shortening time that wound heals by secondary intention with better patient tolerance. Use of pressurised irrigation for wound cleansing is supported by this trial.

Ref. No.: 05060011

P38-Ab0113

The Effectiveness of Therapeutic Play on Pre- and Post-operative Anxiety and Emotional Responses of Hong Kong Chinese Children having Elective Surgery: A Randomized Controlled Trial

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Background: There has been an increase in the use of therapeutic play intervention to help children cope with the stress of hospitalization. However, the majority of previous studies were based on theories and clinical observations; the effectiveness of using therapeutic play in preparing children for surgery has seldom been tested. There is an imperative need for rigorous quantitative research into the efficacy of therapeutic play interventions in preparing children for surgery. This study aimed to examine the effectiveness of therapeutic play intervention in reducing anxiety and negative emotions in children for surgery.

Methods: A randomized controlled trial, two-group pretest and repeated posttest, between subjects design was employed.

A total of 108 children (aged 9-16 years) admitted for elective surgery along with their parents were randomly assigned to the experimental and control groups, with 51 children and their parents receiving therapeutic play intervention (experimental group) and 57 receiving preoperative information preparation (control group). The state anxiety of children and their parents were assessed at pre- and post-operative periods. Children's emotions were documented during anaesthesia induction. Upon discharge home, parents' satisfaction was also assessed. Semi-structured interviews were conducted for selected children, parents and nurses.

Results: The study showed that children receiving therapeutic play intervention reported lower levels of anxiety and exhibited fewer emotions during anaesthesia induction than children receiving preoperative information preparation. Parents in the experimental group reported higher levels of satisfaction than parents in the control group. Results of semi-structure interviews determined the therapeutic play intervention is feasible and acceptable to both health care providers and participants.

Conclusions: The findings of the study generate new knowledge and evidence about therapeutic play intervention, with major clinical implications. The results emphasize the significance of incorporating therapeutic play intervention to provide holistic and quality care to ease the psychological burden of children having surgery. It also promotes the knowledge and understanding among both healthcare professionals and parents that play is of paramount importance to children's lives, and that they need to play even when they are sick.

Ref. No.: 07080981

P39-Ab0061

The Effect of Decision Aids on Treatment Decision Making for Breast Cancer Surgery: A Randomized Controlled Trial

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Background: In Hong Kong, the most common communication practice among surgeons when presenting treatment choices to women facing breast cancer is to pass the decision to her to make. But most women do not want sole responsibility for this decision. Consequently, the stress and difficulty for women faced with treatment decision-making (TDM) is increased resulting in considerable persistent distress. Informational and decision-support strategies are needed to optimize women's breast cancer TDM.

Aims: The aim of this randomized controlled trial was to assess the effect of a decision aid ("DA") on TDM for breast cancer surgery, women's satisfaction with treatment decision, and their post-operative psychological morbidity.

Methods: A total of 276 women who were considering breast cancer surgery for early-stage breast cancer were randomly assigned to receive a DA (take-home booklet) or the standard issue information booklet (control condition) after the initial consultation where the surgeon disclosed the diagnosis and discussed the treatment options with the patients. Randomly 138 were assigned to DA group and 138 were assigned to the control group. Participants completed interview-based questionnaires one-week post-consultation, 4-weeks post-surgery, 4-months post-surgery, and 10-months post-surgery.

Main Outcome Measures: Decision conflict, TDM difficulties, Knowledge of breast cancer and its treatment, Decision regret, Realistic outcome expectation, and Psychological distress.

Results: Women in the DA group had significantly lower decisional conflict (15.8 Vs 19.9, p=0.004) and TDM difficulties (17.5 Vs 19.1, p=0.016) scores compared to women in the control condition. Women receiving the DA had significantly lower decision regret scores over time (b=4.55, p<.05). Knowledge, realistic outcome expectation, and psychological distress were similar between groups.

Conclusions: The DA was beneficial in reducing decisional conflict and TDM difficulties without increasing anxiety levels among women choosing breast cancer surgery. DAs should be considered by surgeons and be integrated into clinical services, specifically as post-consultation decision support.

Ref. No.: 07080651

P40-Ab0051

Assessment of Functional Outcome in Patients Sustaining Moderate and Major Trauma: A Prospective, Multi-centre, Cohort Study

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Introduction and Objectives: Trauma care systems aim to reduce death and to improve functional outcome. Evaluating functional recovery is important as this will facilitate comparison with other settings, assessment of the impact and effectiveness of the system, and provide prognostic information for healthcare workers, patients and relatives. The aim of this study was to describe adult patients' long term overall functional outcome after sustaining moderate and major trauma in Hong Kong.

Methods: Ethical approval was for a prospective, multi-centre, cohort study of adult trauma patients admitted to one of three trauma centres (Prince of Wales Hospital, Queen Elizabeth Hospital and Tuen Mun Hospital), with moderate to severe injury (ISS>9), and surviving to 48 hours. The extended Glasgow Outcome Scale (GOSE; with score=1 for death to =8 for excellent recovery) was used to measure functional outcome from baseline to 2 years after injury. Good outcomes were defined as GOSE>7.

Results: From 1st January 2010 to 30th September 2010, 400 patients were recruited to the study (mean age 53.3 years (range 18-106;70% male)). For patients with ISS 9-15, 64/139(46%) were lost to follow up at 2 years. 8(6%) patients died, no patient was in a vegetative state (GOSE=2), and 38(27%) patients had a GOSE>7. If all patients lost to follow up had GOSE>7, then the maximum possible with good recovery is 102(73%; i.e.(38+64)/139).

For patients with an ISS≥16, 107/261(41%) were lost to follow up at 2 years. 61(23%) patients had died, 1 patient was in a vegetative state (GOSE=2), and 44(17%) patients had a GOSE>7. At 2 years the maximum possible GOSE>7 is 151 (58%; i.e. (44+107)/261).

Conclusions: Two years after injury, 6 to 23% patients had died, and 17 to 27% had a good recovery. The overall possibility of a good recovery could reach 58 to 73%.

Ref. No.: 07080261

P41-Ab0005

A Study on Health-related Quality of Life of Patients with Colorectal Neoplasm and Cost-Effectiveness Analysis of Colorectal Cancer Screening in Hong Kong

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Background: Colorectal cancer (CRC) is the most common cancer in Hong Kong. Health-related quality of life (HRQOL) is an important health outcome of CRC survivors. Screening for CRC has the potential of preventing CRC death but there was uncertainty on its impact on HRQOL and the cost-effectiveness of different screening strategies.

Aims and Objectives: To determine the HRQOL and health preference of patients with colorectal neoplasms (CRN) including polyps, and to evaluate the cost-effective CRC screening strategies in terms of QALY gained compared to no screening.

Methods: A longitudinal study on the HRQOL of CRN patients over 12 months with 3 evaluations at six-monthly intervals. Each patient completed the Functional Assessment of Cancer Therapy-Colorectal, version 2 of the Short-Form 12-item Health Survey (SF-12) and SF-6D and a structured questionnaire on socio-demographic data. HRQOL scores of CRN patients were compared to those of the general population and by different CRN disease stages. The associations of HRQOL with socio-demographics and disease-related factors, and the change of HRQOL over 12 months were explored. The health preference scores by CRN disease stages and direct medical costs of subjects of the HRQOL study were applied together with survival data extracted from the literature to a Markov model to evaluate the cost-effectiveness of 5 different CRC screening strategies against no screening in terms of QALYs gained.

Results: 554, 479 and 414 patients completed the baseline, six months and 12 months survey, respectively. Overall patients with stable CRN reported worse SF-12 physical summary scores but better SF-12 mental summary and similar SF-6D health preference scores than those of the HK general population. Disease stage at diagnosis was the most significant determinant of HRQOL of CRN patients. Rectal cancer was associated with worse physical HRQOL and health preference scores. Immunochemical faecal occult blood (I-FOBT) two-yearly was the most cost-effective screening strategy at an ICER of HK$43,660 per QALY compared to no screening. Annual I-FOBT was more effective than biennial I-FOBT but more expensive with an ICER of HK$51,610 per QALY. The ICER/QALY of both are below the UK NICE benchmark of GBP20, 000 (~HKD$240,000) or the HK 2013 annual GDP of ~HKD$260,000.

Conclusions: HRQOL of Chinese patients with stable CRN, except those with advanced (stage III and IV) cancers, were comparable to the general population norm in HK. Biennial I-FOBT and annual I-FOBT are cost-effective CRC screening strategies for the HK general Chinese population.

Ref. No.: 08090851

P42-Ab0048
Optimizing Resource Allocation for Breast Cancer Prevention and Care among Hong Kong Chinese Women: A Generalized Cost-effectiveness Analysis

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Background and Objectives: Recommendations about funding of interventions through the full spectrum of the disease have often been made in isolation or been derived in separate single-intervention analyses. We primarily evaluated and optimized budgetary allocations by comparing cost-effectiveness data for the selected preventive and management strategies throughout the disease course for breast cancer in HK Chinese women.

Methods: We developed a bio-mathematical model and evaluated the deployment of additional resources for breast cancer treatment related interventions, under the decision analytic rubric. Nesting a state-transition Markov model within a generalized cost-effectiveness analytic framework, we compared costs and quality-adjusted life years (QALYs) to estimate average cost-effectiveness ratios for the following interventions at the population level: biennial mass mammography (from 40 to 69 or 79 years), reduced waiting time for post-operative radiotherapy (by 15 or 25%), adjuvant endocrine therapy (either upfront aromatase inhibitor (AI) therapy or sequentially/switching with tamoxifen and AI use) in postmenopausal estrogen receptor positive disease, targeted immunotherapy in HER2 over-expressed disease, and enhanced palliative services (either at home or as an inpatient). Usual care for eligible patients in the public sector was the comparator.

Results: From strategies we considered, the optimal allocation of additional resources for breast cancer would sequentially be: a 25% reduction in waiting time for postoperative radiotherapy (average cost-effectiveness ratio = US$5,000 per QALY); an enhanced, home-based palliative care (US$7,105 per QALY); adjuvant, sequential endocrine therapy (US$17,963 per QALY); targeted immunotherapy (US$62,092 per QALY); and mass mammography screening of women ages 40 to 69 years (US$72,576 per QALY).

Discussion: Given the situation in Hong Kong, it appears that it is more cost-effective to provide women with the most intensive treatment and care after diagnosis of breast cancer than to offer young women mammography. Future research should focus how to deploy these decisions flexibly to fit various budgetary constraints, affordability of cancer medicines and ethical considerations. Our results could further inform policy debates about resource allocation on service delivery regarding breast cancer diagnosis, treatments palliative care and prevention locally.

Ref. No.: 09100921

P43-Ab0072
A Randomized Control Trial to Evaluate Self-Sampling as A Primary Cervical Screening Test in Women

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Background and Aims: The causal relation between Human papillomavirus (HPV) and cervical cancer has enabled HPV DNA self-sampling to be a possible cervical screening method. This study investigated whether it could be an alternative approach by examining: 1) The uptake rate of cervical cancer screening; 2) The acceptability and confidence of self-sampling method; 3) The rate of cervical intraepithelial neoplasia grade 2+ (CIN2+) in screening; 4) Detection between self-collected samples and Pap smear; 5) The costing between self-sampling and Pap smear.

Methods: All participants would adopt both screening methods, to minimize the sequence effect of screening methods, a crossover randomized controlled trial was conducted. Participants were allocated to 2 arms (Arm 1: self-sampling before a Pap smear, Arm 2: Pap smear before self-sampling). Women were also assessed their attitudes toward and intentions to the future use of HPV DNA self-sampling.

Results: A total of 392 participants were recruited. Participants generally accepted self-sampling as an alternative as clinician-sampling (overall score 7.8 and 7.7 respectively), in particular, participants without previous experience of Pap smears preferred self-sampling ($p < 0.001$). In general, participants had significantly more positive feelings on self-sampling with less anxious, less uncomfortable, more pleasant, less embarrassed, more relaxed, less painful, and less invasion of privacy ($p < 0.001$). However, participants trusted Pap test results more and had more confidence in collection than self-sampling ($p < 0.001$). Among 12 abnormal Pap smear results diagnosed, only 1 was confirmed with CIN 1. The prevalence of HPV was 11.7 % (95% CI, 8.8 to 15.4) with self-collected samples and 7.7% (95% CI, 5.3 to 10.9) with clinician-collected samples. The overall agreement between two screening methods was 93.9% and agreement among the positives was 52.0%, with a kappa of 0.65 (95% CI of 0.52-0.78). We estimated that the introduction of HPV DNA self-sampling could increase the future rate of uptake of cervical cancer screening by 6.5%, from 61.7% to 65.7%, and would entail lower costs. The difference of costs of two methods was estimated as HKD 645.28 per case with initial screening.

Conclusions: The high rate of detection and acceptance, and the lower cost of HPV DNA testing suggest it could be an alternative cervical screening method to overcome the barriers to Pap smears, and enhance the coverage of cervical cancer screening. Prospective study is needed to evaluate the feasibility of HPV self-sampling and performance in the context of population based screening programme.

Ref. No.: CU-10-04-02

P44-Ab0078
Long-term Efficacy of a Motivational Enhancement Education Program on Continuous Positive Airway Pressure Adherence in Obstructive Sleep Apnea: A Randomized Controlled Trial

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Introduction: Long term continuous positive airway pressure (CPAP) treatment has been shown to alleviate symptoms and prevent health-related consequences in subjects with obstructive sleep apnea (OSA). Poor adherence to CPAP treatment adversely affects the effectiveness of this therapy. CPAP education is important to enhance CPAP adherence. This randomized controlled trial (RCT) aimed to examine the efficacy of a brief motivational enhancement education program in improving CPAP adherence in OSA subjects after 1 year of CPAP treatment.

Methods: Newly diagnosed OSA subjects were recruited into this RCT. The control group received usual advice on the importance of CPAP therapy and its care. Intervention group received usual care plus brief motivational enhancement education directed at enhancing subjects' knowledge, motivation and self-efficacy to use CPAP. This education program included a 25-minute video, a 20-minute patient-centered interview and a 10-minute telephone follow-up (Figure 1). CPAP compliance data were recorded in the CPAP machine, and downloaded at 1 month, 3 months and 1 year after CPAP treatment. The primary outcome was CPAP usage, and the secondary outcomes were self-reported daytime sleepiness [Epworth Sleepiness scale (ESS)], health-related quality of life [Calgary sleep apnoea quality of life index, Short Form (36) Health Survey, Functional outcomes of sleep questionnaire], and mood (Depression anxiety stress scale 21), and blood pressure.

Results: 100 OSA subjects were recruited, with a mean±SD age of 52±10 years, ESS 9±5, median Apnea Hypopnea Index of 29 (20, 53) events/hour. The intervention group had better CPAP usage compared to the control group, higher daily CPAP usage by 2 hours/day (p<0.001); a five-fold in the number of subjects using CPAP for ≥70% of days with ≥4 hours per day (p<0.001)], and a greater improvement in daytime sleepiness (ESS) by 2.1 units (p=0.002) at 1 year. No significant differences were found in blood pressure, health-related quality of life and mood.

Conclusions and Discussion: OSA subjects who received motivational enhancement education in addition to the usual care had better CPAP adherence than the usual care alone, with a greater improvement in daytime sleepiness after 1 year of treatment. A simple motivational enhancement education programme (one face-to-face session and one telephone follow-up) is able to utilize limited-time and -manpower resources to enhance CPAP adherence, with clinical improvement in subjects with OSA.

Ref. No.: 09101291

P45-Ab0104

Protocol-Driven Adjustment of Ocular Hypotensive Medication in Patients at Low Risk of Conversion to Glaucoma

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Aims: To investigate the safety and potential savings of decreasing medication use in low-risk ocular hypertensive (OH) patients.

Methods: OH patients receiving pressure-lowering medication identified by medical record review at a university hospital underwent examination by a glaucoma specialist with assessment of visual field (VF), vertical cup-disc ratio (vCDR), central corneal thickness (CCT) and IOP. Subjects with estimated 5-year risk of glaucoma conversion <15% were asked to discontinue ≥1 medication, IOP was re-measured one month later.

Results: Among 212 eyes of 126 patients, 44 (20.8%) had 5-year risk >15% and 14 (6.6%) had unreliable baseline VF. At one-month, 15 patients (29 eyes, 13.7%) defaulted follow-up or refused to discontinue medication and 11 eyes (5.2%) had risk > 15%. The remaining 69 patients (107 eyes, 50.7%) successfully

discontinued 141 medications and completed 1-year follow-up. Mean IOP (20.5 ± 2.65 mmHg versus 20.3 ± 3.40, p = 0.40) did not change, though mean visual field pattern standard deviation (1.58±0.41 dB versus 1.75±0.56 dB, p = 0.001) and glaucoma conversion risk (7.31±3.74% versus 8.76±6.28%, p = 0.002) increased at one year. Mean defect decreased (-1.42 ± 1.60 versus -1.07 ±1.52, p = 0.025). One eye (0.47%) developed a repeatable visual field defect and 13 eyes (6.1%) had 5-year risk > 15% at 1 year. The total one-year cost of medications saved was USD4,596.

Conclusions: Nearly half (43.9%) of low risk OH eyes in this setting could safely reduce medications over one year, realizing substantial savings.

Ref. No.: 07080601

P46-Ab0031

Professional Breastfeeding Support for First-time Mothers: A Multicentre Cluster Randomised Controlled Trial

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Objective: To evaluate the effect of two postnatal professional support interventions on the duration of any and exclusive breastfeeding.

Design: Multicentre, three-arm, cluster randomised controlled trial.

Population: A cohort of 722 primiparous breastfeeding mothers with uncomplicated, full-term pregnancies.

Methods: The three study interventions were: (1) standard postnatal maternity care; (2) standard care plus three in-hospital professional breastfeeding support sessions, of 30-45 minutes in duration; or (2) standard care plus weekly post-discharge breastfeeding telephone support, of 20-30 minutes in duration, for 4 weeks. The interventions were delivered by four trained research nurses, who were either highly experienced registered midwives or certified lactation consultants.

Main outcome measures: Prevalence of any and exclusive breastfeeding at 1, 2, and 3 months postpartum.

Results: Rates of any and exclusive breastfeeding were higher among participants in the two intervention groups at all follow-up points, when compared with those who received standard care. Participants receiving telephone support were significantly more likely to continue any breastfeeding at 1 month (76.2 versus 67.3%; odds ratio, OR 1.63, 95% confidence interval, 95% CI 1.10-2.41) and at 2 months (58.6 versus 48.9%; OR 1.48, 95% CI 1.04-2.10), and to be exclusively breastfeeding at 1 month (28.4 versus 16.9%; OR 1.89, 95% CI 1.24-2.90). Participants in the inhospital support group were also more likely to be breastfeeding at all time points, but the effect was not statistically significant.

Conclusions: Professional breastfeeding telephone support provided early in the postnatal period, and continued for the first month postpartum, improves breastfeeding duration among first-time mothers. It is also possible that it was the continuing nature of the support that increased the effectiveness of the intervention,

rather than the delivery of the support by telephone specifically.

Ref. No.: 07080881

P47-Ab0115
Person-centred Care for Demented Older Adults: A Qualitative Analysis

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Background: Along with the rapid pace of an aging society in Hong Kong, the demand for dementia care has placed increasing pressure on the long-term care service sector. A scientific care approach is urgently needed to ensure quality of care. Person-centred care (PCC) has been shown to be the "most desirable" option for older adults with dementia. Yet, how PCC is conceptualised and practiced in Hong Kong remains unknown.

Objectives: This study aims to explore stakeholders' attitudes towards PCC for elderly patients with dementia in Hong Kong.

Methods: A qualitative research method was adopted: Eight focus groups and eight in-depth interviews among four groups of stakeholders (e.g., professional formal caregivers, nonprofessional formal caregivers, family caregivers, and mildly cognitively impaired older adults) were conducted. Guidelines were developed based on Brooker's PCC=V+I+P+S model and were supplemented by a tripartite model of attitude.

Results: Formal care providers believed that PCC provided both holistic care and respect for the dignity of older adults, in line with their professional ethics, vision, and mission. However, family caregivers were unfamiliar with the concept of PCC. In contrast to formal care providers, they believed that "professionalised" formal care could be strengthened. With regard to affection associated with PCC, formal care providers were both familiar and positive towards the affective component of PCC, but were somewhat ambivalent when they failed to achieve "PCC." On the contrary, family members felt unfamiliar with PCC. After the meaning of PCC was explained, they expressed positive feelings towards the concept, but were still notably distant from full acceptance. With regard to the practice of PCC by stakeholders, there were a series of good practices that were in line with PCC principles. Meanwhile, although informal caregivers showed high tendencies of infantilising older adults with dementia, they proactively communicated with formal caregivers in order to achieve personalised care.

Conclusions: Diverse attitudes towards PCC were observed among stakeholders concerning their perceptions, affections, and practices. These diverse attitudes could be rooted in cultural and contextual determinants (e.g., family caregivers' attitudes of relying on authority and a lack of policy framework for dementia care). Finally, we discuss implications for policy and service development.

Ref. No.: 09101241

P48-Ab0020
Quality of Life and Symptom Measurements in Chinese Women with Pelvic Floor Disorders: Validation Study of Pelvic Floor Distress Inventory (PFDI) and Pelvic Floor Impact Questionnaire (PFIQ)

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Objective: The reliability, validity and responsiveness of Pelvic Floor Distress Inventory (PFDI) and Pelvic Floor Impact Questionnaire (PFIQ) in Chinese women suffering from pelvic floor disorders (PFD) were investigated.

Methods: Chinese women with PFD filled in the Chinese PFDI and PFIQ and Short Form Health Survey (SF-36). Both the women and the attending gynecologist were asked independently to grade the overall severity of symptoms on a visual analogue scale (VAS). They completed a 3-days urinary and faecal diary, and were followed by urodynamic studies (UDS) and/or anal manometry and anal ultrasonography where appropriate.

After four weeks, the women recruited in the first 6 months repeated the questionnaires. All were not offered any treatment during this interval. 156 women were assessed again after they received continence surgery and/or pelvic floor repair (PFR) surgery, or vaginal pessary.

Results: 597 women, aged 55.0 ± 11.3 years and parity 2.7 ± 1.5, completed the study. Among them, 54.4% had urinary incontinence (UI) only, 32.2% had both UI and pelvic organ prolapse (POP), 10.9% had POP only, 2.2% had UI and FI and 0.3% had UI, FI and POP.

Reliability: The Cronbach's alpha of PFDI and PFIQ was 0.92 and 0.98, indicated that both had high internal consistency. The intraclass correlation coefficient of PFDI and PFIQ was 0.77 and 0.79, indicated that the test-retest reliability was acceptable.

Convergent validity: There were significant negative correlation between PFDI and PFIQ and SF-36. The staging of POP was positively correlated with POPDI and POPIQ. Daytime voiding frequency was positively correlated with UDI and UIQ. No abnormality detected group had significantly lower UDI score than the USI or DO group. The frequency of FI episode was positively correlated with CRADI and CRAIQ. Both women's and gynaecologist's VAS score was positively correlated with PFDI and PFIQ.

Responsiveness: There were significant improvements in the respective subscales of PFDI and PFIQ, demonstrating moderate to great responsiveness after treatments. The minimal clinically important change (MCIC) of UDI and UIQ for women who underwent continence surgery and POPDI, POPIQ, UDI, UIQ, CRADI and CRAIQ for women who underwent PFR surgery or vaginal pessary were also established.

Conclusions: The Chinese PFDI and PFIQ were valid and reliable for use. Its responsiveness was established. The MCIC of UDI and UIQ for women who underwent continence surgery and POPDI, POPIQ, UDI, UIQ, CRADI and CRAIQ for women who underwent PFR surgery or vaginal pessary were also established.

Ref. No.: 07080621

P49-Ab0001
Safety Studies on Commonly Used Chinese Herbal Medicines during Pregnancy

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Introduction: It is still unknown how safe Chinese herbal medicines are being used during pregnancy and if there is any effects on embryo-fetal development and prenatal and postnatal growth. We aimed to determine safety of Chinese herbal medicines during pregnancy by screening any beneficial and adverse effects of commonly used Chinese herbal medicines on mothers and conceptuses.

Methods: Reproductive toxicity of medicinal products in pregnant ICR mice will be determined accordingly to FDA guidelines. Most commonly used Chinese herbal medicines during pregnancy were selected and administrated at relevant clinical doses to pregnant mice at various gestational stages, including implantation, gastrulation, organogenesis, maturation and whole gestation periods in vivo. Embryotoxicity were confirmed by whole embryo culture ex vivo. Immediate and latent effects of the exposure during and after pregnancy on mothers and conceptuses,maternal effects on weight changes, implantation failure and fetal resorption and perinatal effects on developmental delay, growth restriction and congenital malformations were studied.

Results: Adverse pregnant outcomes are more common than favourable outcomes. Maternal, prenatal and postnatal adverse outcomes were significantly increased in maternal exposure of the test Chinese medicines during pregnancy. The adverse effects included decreased maternal weight gain, embryo growth and development and postnatal weight gain; and increased maternal mortality, early fetal resorption, congenital skeletal malformations and perinatal mortality.

Conclusions: Potential reproductive toxicity of some commonly used Chinese herbal medicines was identified within clinical dose in mice. Caution should be taken in the clinical applications of those Chinese medicines during pregnancy.

Ref. No.: 06070511

P50-Ab0126
Can Botulinum Toxin Decrease Carer Burden in Long-term Care Residents with Upper Limb Spasticity? A Randomized Controlled Study

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Objectives: To evaluate whether botulinum toxin can decrease the burden for carers of long term care patients with severe upper limb spasticity.

Methods: This was a double-blind placebo-controlled trial with a 24-week follow up period.

Setting: A 250-bed long term care hospital, the infirmary units of 3 regional hospitals, and 5 care and attention homes.

Participants: 55 long-term care patients with significant upper limb spasticity.

Interventions: Patients were randomized into two groups that received either intramuscular botulinum toxin A or saline. All patients received concurrent standardized physical therapy and occupational therapy programs.

Main Outcome Measures: The primary outcome measure was provided by the carer burden scale. Secondary outcomes included goal attainment scale (GAS), measure of spasticity by modified Ashworth score (MAS), passive range of movement (PROM) for shoulder abduction, elbow extension and finger extension. Pain was assessed using the Pain Assessment in Advanced Dementia (PAINAD) Scale.

Results: 55 patients (21 males; mean age=69, SD=18) were recruited. A week 6 post-injection, there was a significant decrease in the carer burden scale in the treatment group compared with the placebo group. 18/30 (60%) patients in the treatment group versus 2/25(8%) patients in the control group had a significant 4-point reduction of carer burden scale ($P<0.001$). There was also significant improvement in the GAS, as well as the MAS, resting angle and PROM of the 3 regions (shoulder, elbow and fingers) in the treatment group which persisted until week 24. No significant difference in PAINAD scale was found between the two groups. No serious botulinum toxin type A related adverse effects were reported.

Conclusions: Long-term care patients who were treated for upper limb spasticity with intramuscular injection of botulinum toxin A had significant improvements in muscle tone and joint mobility, and care-givers were able to perform basic upper limb care more easily.

Ref. No.: 07081271

P51-Ab0003
Dense Cranial Electroacupuncture Stimulation for Major Depressive Disorder: A Single-Blind, Randomized, Controlled Study

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Background: Previous studies suggest that electroacupuncture possesses therapeutic benefits for depressive disorders. The purpose of this study was to determine whether dense cranial electroacupuncture stimulation (DCEAS) could enhance the antidepressant efficacy in the early phase of selective serotonin reuptake inhibitor (SSRI) treatment of major depressive disorder (MDD).

Methods: In this single-blind, randomized, controlled study, patients with MDD were randomly assigned to 9-session DCEAS

or noninvasive electroacupuncture (n-EA) control procedure in combination with fluoxetine (FLX) for 3 weeks. Clinical outcomes were measured using the 17-item Hamilton Depression Rating Scale (HAMD-17), Clinical Global Impression-severity (CGI-S), and Self-rating Depression Scale (SDS) as well as the response and remission rates.

Results: Seventy-three patients were randomly assigned to n-EA (n = 35) and DCEAS (n = 38), of whom 34 in n-EA and 36 in DCEAS group were analyzed. DCEAS-treated patients displayed a significantly greater reduction from baseline in HAMD-17 scores at Day 3 through Day 21 and in SDS scores at Day 3 and Day 21 compared to patients receiving n-EA. DCEAS intervention also produced a higher rate of clinically significant response compared to n-EA procedure (19.4% (7/36) vs. 8.8% (3/34)). The incidence of adverse events was similar in the two groups.

Conclusions: DCEAS is a safe and effective intervention that augments the antidepressant efficacy. It can be considered as an additional therapy in the early phase of SSRI treatment of depressed patients.

Ref. No.: 06070831

P52-Ab0023
Complete Genome Sequence Analysis of Human Enterovirus 71 Strains from 2004 to 2010 in Hong Kong

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Background: Enterovirus 71 (EV71) is a common etiological agent of hand, foot and mouth disease (HFMD) in children. EV71 epidemics have been reported in Hong Kong in recent years, and yet the genetic information of EV71 strains circulating in our locality is limited. The objective of this study was to investigate the genetic evolution of these EV71 isolates in Hong Kong over a 7-year period.

Methods: Twenty-two EV71 isolates from Hong Kong during 2004-2010 were included for phylogenetic analysis using partial VP2-VP3, 2C and 3D regions. Eight EV71 strains were selected for complete genome sequencing and recombination analysis.

Results: Among the 22 EV71 isolates, 20 belonged to subgenotype C4 and 2 belonged to subgenotype C2 based on the phylogenetic analysis of partial VP2-VP3, 2C and 3D gene regions. Phylogenetic, similarity plot and bootscan analyses using complete genome sequences of seven EV71 isolates of subgenotype C4 supported that the "double-recombinant" strains of subgenotype C4 persistently circulating in Hong Kong should belong to a newly proposed genotype D. Further analysis revealed two clusters, subgenotypes C4b and C4a (proposed genotypes D1a and D1b respectively), with "genotype D1b" strains being predominant in recent years in Hong Kong. A distinct lineage of EV71 subgenotype C2 has emerged in Hong Kong in 2008. The evolutionary rate of EV71 was 3.1×10^{-3} nucleotide substitutions per site per year similar to that of other enterovirus, such as EV68, but was relatively lower than those of echovirus 30 and poliovirus. Molecular clock analysis using VP1 gene dated the time to the most recent common ancestor of all EV71 genotypes to 1900s, while the EV71 "double-recombinant" strains of "genotype D" were detected as early as 1998.

Conclusions: This study provides the molecular basis for proposing a new "genotype D" of EV71 and assigning a discrete lineage of subgenotype C2. EV71 strains of "genotype D" have

been circulating in Hong Kong for over 7 years, with "genotype D1b" being predominant. Given that mutation and recombination are common phenomena in enterovirus evolution, continuous surveillance by sequencing of at least 3 gene regions (probably one from P1, one from P2 and one from P3) or whole genome is of paramount importance in identifying new types or recombinants of EV71 with epidemic potential in the future.

Ref. No.: 11101142

P53-Ab0017
Association between HLA-B*1502 Allele and Antiepileptic Drugs-induced Severe Cutaneous Reactions in Han Chinese: A Hong Kong-wide Population-based Study

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Introduction: HLA-B*15:02 screening is recommended before starting carbamazepine in Han Chinese and South-East Asians because the allele is strongly predictive of Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) induced by the drug. We examined whether other HLA-B alleles are also involved and whether the association extends to other antiepileptic drugs (AEDs).

Methods: Cases of SJS/TEN induced by any AEDs were recruited and matched (1:5) with AED-tolerant controls. Carrier rates of HLA-B alleles, determined by direct sequencing, were compared between cases and controls. Results were meta-analyzed with previous studies to examine the associations between HLA-B*15:02 and SJS/TEN induced by phenytoin and lamotrigine.

Results: A total of 55 cases (27 carbamazepine, 15 phenytoin, 6 lamotrigine, 7 other AEDs) and 275 controls were recruited. In drug-specific analysis, the carrier rate of HLA-B*15:02 was significantly higher in carbamazepine-SJS/TEN cases compared with carbamazepine-tolerant controls (92.3% vs. 11.9%; p=3.51X10-18; OR 89.25; 95% CI 19.25-413.83), and also in phenytoin-SJS/TEN cases compared with phenytoin-tolerant controls (46.7% vs. 20.0%; p=0.045; OR 3.50; 95% CI 1.10-11.18). Meta-analyses showed a strong association of HLA-B*15:02 with phenytoin- (p<3X10-4; OR 4.26; 95% CI 1.93-9.39) and, to a lesser extent, lamotrigine-SJS/TEN (p=0.03; OR 3.59; 95% CI 1.15-11.22). Compared with drug-tolerant controls, the carrier rates of HLA-B*40:01 and HLA-B*58:01 were lower in cases of SJS/TEN induced by carbamazepine (p=0.004) and other AEDs (p=0.009), respectively.

Conclusions: SJS/TEN induced by carbamazepine and phenytoin is strongly and moderately associated with HLA-B*15:02 in Han Chinese, respectively. Possible protective associations with HLA-B*40:01 and HLA-B*58:01 warrant further investigation.

Ref. No.: 07080381

P54-Ab0006
Mechanistic Studies on Bakuchiol and Macrocarpal C with Regard to Their Anti-dermatophyte Effects *In Vitro* and Tinea Pedis-treating Activities *In Vivo*

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Introduction: Tinea pedis is a dermatophyte infection of the feet mainly caused by *Trichophyton mentagrophytes* and *Trichophyton rubrum*. When infected, the interdigital spaces and other skin areas of the feet are pruritic, scaling, and can be complicated with secondary bacterial infections. It is among the most prevalent skin infections diagnosed in different regions of the world. Albeit not life-threatening, this disease can markedly affect the quality of life and well-being of the patients.

Aims and Objectives: Bakuchiol and macrocarpal C are two active antifungal compounds isolated from Psoraleae Fructus (補骨脂) and Eucalypti Globuli Folium (藍桉), respectively. The present study aimed to investigate the underlying mechanisms and the therapeutic effect of bakuchiol and macrocarpal C in *T. mentagrophytes*-induced tinea pedis.

Methods: For elucidating the action mechanisms, three *in vitro* assays were performed. They include (i) fungal membrane permeability test using SYTOX® Green; (ii) reactive oxygen species (ROS) production using cell-permeable fluorogenic probe 5-(and-6)-carboxy-2',7'-dihydrodichlorofluorescein diacetate; and (iii) DNA fragmentation detected by terminal deoxynucleotidyl transferase dUTP nick-end labeling (TUNEL). In parallel, a guinea pig model of tinea pedis was employed to evaluate the *in vivo* efficacy of bakuchiol and macrocarpal C.

Results: *In vitro* mechanistic studies demonstrated that both bakuchiol and macrocarpal C could increase membrane permeability and ROS production in fungal cells. Moreover, macrocarpal C, but not bakuchiol, was also able to induce DNA fragmentation in the dermatophytes. In guinea pig model of tinea pedis, bakuchiol at 1%, 5% or 10% (w/w) in aqueous cream could significantly reduce the fungal burden of infected feet ($p < 0.01$-0.05). However, its effect was inferior to commercial antifungal Lamisil® cream. On the other hand, macrocarpal C was ineffective in treating tinea pedis *in vivo*.

Conclusions: Bakuchiol and macrocarpal C were promising in inhibiting the *in vitro* growth of *T. mentagrophytes* via different mechanisms. However, their efficacies in treating tinea pedis in guinea pig model were weak.

Implications: Results of present study provided basic scientific support to reveal the anti-fungal activities and action mechanisms of bakuchiol and macrocarpal C in inhibiting the growth of dermatophytes. However, owing to their inferior effects in animals, much more works (e.g. dosing regimen, product formulation refinement) need to be done in order to further develop these two compounds into topical antifungal drugs for clinical use.

Ref. No.: 10090502

P55-Ab0024

Exploring the Potential of Sophora Flavescens (Ku-Shen) as a Booster for Antiretroviral Therapy through Cytochrome P450 3A4 Inhibition

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Introduction: *Sophora flavescens,* or Ku-Shen in Chinese, is a Chinese medicinal herb commonly used for the treatment of gastrointestinal hemorrhage, skin diseases, pyretic stranguria and viral hepatitis. It has been shown in a previous study that Sophora flavescens possessed strong CYP3A4 inhibitory activity. It was therefore hypothesized that Sophora flavescens could be able to increase the plasma concentration of the anti-HIV drug, thereby potentiating ("boosting") their therapeutic effects.

Objectives: This study aimed to explore the potential herb-drug interactions between *S. flavescens* and indinavir, a protease inhibitor for HIV treatment.

Methods and Results: Concomitant oral administration of *Sophora* extract (0.158 g/kg or 0.63 g/kg, p.o.) and indinavir (40 mg/kg, p.o.) in rats twice a day for 7 days surprisingly resulted in a dose-dependent decrease of plasma indinavir concentrations, with 55%-83% decrease in AUC0-∞ and 38%-78% reduction in C_{max}. The CL (Clearance)/F (fraction of dose available in the systemic circulation) increased up to 7.4-fold in *Sophora*-treated rats. Treatment with oxymatrine, an alkaloid compound derived from S. flavescens (45 mg/kg, p.o.) also decreased indinavir concentrations, while the ethyl acetate fraction of *Sophora* extract had no effect. Urinary indinavir (24-h) was reduced, while the fraction of indinavir in faeces was increased after *Sophora* treatment. Compared to the controls, multiple dosing of *Sophora* extract elevated both mRNA and protein levels of P-gp in the small intestine and liver. In addition, *Sophora* treatment increased intestinal and hepatic mRNA expression of CYP3A1, but had less effect on CYP3A2 expression. Although protein levels of CYP3A1 and CYP3A2 were not altered by *Sophora* treatment, hepatic CYP3A activity increased in the *Sophora*-treated rats.

Conclusions and Discussion: Our experimental data demonstrated that *Sophora flavescens* reduced plasma indinavir concentration after multiple concomitant doses, possibly through hepatic CYP3A activity and induction of intestinal and hepatic P-gp. The animal study would be useful for predicting potential interactions between natural products and oral pharmaceutics and understanding the mechanisms prior to human studies. Results in the current study suggest that patients using indinavir might be cautioned in the use of *S. flavescens* extract or *Sophora*-derived products.

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P56-Ab0029

Long-term Neurocognitive Outcomes of Children Prenatally Exposed to Low-dose Methylmercury

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Introduction: International studies suggest that low dose prenatal methylmercury exposure (>29 nmol/L) is associated with long-term adverse neurocognitive effects. There is evidence that due to high maternal fish consumption, many children in Hong Kong exceed this level.

Objectives: To study whether there are any associations between prenatal methylmercury exposure and adverse neurocognitive outcomes in Hong Kong children.

Methods: Children from the original birth cohort (1057 children) were eligible. Children with conditions that would affect neurocognitive development, but were unrelated to methylmercury exposure were excluded. Subjects were assessed

by a wide panel of tests covering a broad range of neurocognitive functions: Hong Kong Wechsler Intelligence Scale for Children (HK-WISC), Hong Kong List Learning Test (HKLLT), Tests for Everyday Attention for Children (TEACH), Boston Naming Test, and Grooved Pegboard Test.

Results: 608 subjects were recruited (median age 8.2 years, IQR 7.3, 8.8; 53.9% boys). Multivariate analysis correcting for factors including child age and sex did not reveal consistent associations, however, after standardising the neurocognitive outcome subtest scores it was found that cord blood mercury concentration was significantly associated with three subtests: Picture Arrangement of HK-WISC (coefficient -0.944, P=0.049) and Short and Long Delay Recall Difference of the HKLLT (coefficient -1.087, P=0.007 and coefficient -1.161, P=0.005, respectively), i.e., performance worsened with increasing prenatal methylmercury exposure in these subtests.

Discussion: Small, but statistically significant adverse associations between prenatal methylmercury exposure and long-term neurocognitive effects (a visual sequencing task and retention ability of verbal memory) were found in our study. These effects are comparable with studies with higher prenatal methylmercury exposure levels and suggest that safe strategies to further reduce exposure levels in Hong Kong may be warranted.

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P57-Ab0046

Effects of Ventilation Schemes and Heat Sources on the Effectiveness of Upper-room Ultraviolet Germicidal Irradiation in Hospital or Health Care Facilities

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Introduction: The inactivation effect of the ultraviolet germicidal irradiation (UVGI) with optimal wavelength ranging from 250–270 nm (UV-C) on microorganisms has been well demonstrated in the past few decades. One successful application of UVGI is to irradiate the upper part of a room while minimizing human exposure at the lower part of the room to avoid overdose through the skin and eyes. This is known as the upper-room UVGI system. There has been an increasing interest in the use of the upper-room UVGI system because of its proven disinfection effect for microorganisms. To better design and explore further potential applications of UVGI systems, optimizing the conditions to use the system in enclosures is of critical importance.

Objectives: This study aimed to develop a novel mathematical model for optimizing the design of the indoor upper-room UVGI system in disinfecting microorganisms to reduce the transmission of infectious diseases in hospital and health care facilities.

Methods: A model was developed to predict the spatial UVGI intensity in a space and evaluate the spatial distribution of indoor microorganisms and the inactivation performance of microorganisms under the UVGI system. The model was validated by laboratory-scale experiments. The modeling results were then compared with the experimental results and used to examine the influential parameters.

Results: The UVGI intensity predicted by the model agreed very well with the lab-scale experimental measurements. By applying the model, the predicted microorganism distribution under both the UVGI system and ventilation also agreed well with the experimental measurements. A number of influential parameters are discussed in this study, including the ventilation scheme,

number of units, susceptibility of microorganisms, installation orientation (relative to the diffusers) and number of occupants. Field measurements taken in an elderly center confirmed the efficiency of the upper-room UVGI system on microorganisms inactivation. Based on these results, detail discussion on applying the upper-room UVGI system for hospital or health care facilities is highlighted.

Conclusions: A novel and accurate model which predict the inactivation performance of the upper-room UVGI system on bioaerosols under different conditions was developed.

Implications: This model has great potential for optimizing the design of the indoor upper-room UVGI systems.

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P58-Ab0085

Acute Adverse Events from Over-the-counter Chinese Herbal Medicines: A Population-based Survey of Hong Kong Chinese

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Background: Although over-the-counter traditional Chinese herbal medicine (COTC) is commonly used to treat everyday illness in many parts of the world, no population-based study has been done to examine the prevalence and factors associated with COTC-related adverse events.

Methods: A cross-sectional telephone survey was conducted among Hong Kong Chinese adults in 2011 (n = 1100) with informed verbal consent. Stepwise logistic regression of demographic, attitudinal and behavioral variables was used to determine factors associated with past-year adverse events.

Results: Of study respondents, 71.7% (789/1100) reported past-year COTC use and 2.3% (25/1100) reported at least one COTC-related adverse event in the past year. Of the 27 adverse events cases reported among COTC users, the most common were allergic reactions (n = 11) dizziness (n = 5), and gastro-intestinal problems (n = 4). Pills/capsules were the dosage form that caused the highest proportion of adverse events (n = 10), followed by plasters (n = 7), creams/ointments (n = 5), and ingestible powders (n = 2).Although COTC users reporting adverse events were more likely to report greater practices to avoid adverse events (OR = 6.47; 95% CI: 1.38-30.3); they were also more likely to possess lower education levels (OR = 9.64, 95% CI: 2.20-42.3) and to have received COTC information from non-reliable, mass-media information sources such as magazines (OR = 3.32; 95% CI: 1.01-8.50) or television (OR = 2.93; 95% CI: 1.03-10.7). Package labels were also felt to be unclear by 42.9% of COTC users. A large proportion of COTC users demonstrated low levels of COTC-related knowledge, while the main impediment to greater information-seeking was the belief that reliable COTC information is not obtainable from Western health professionals.

Conclusions: Despite global movements toward more stringent complementary medicine regulation, the limited accessibility of reliable information and widespread misperceptions among consumers present major challenges for the safe use of complementary medicine.

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P59-Ab0109
Comparing Prednisolone and Indomethacin in Treating Clinical Gouty Arthritis: Multi-centre, Double-Blind, Randomized Trial

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Aims: To compare the analgesic efficacy and safety of oral prednisolone and oral indomethacin in the acute management of gout-like arthritis

Study Design: Four centres, double-blind, randomised equivalence trial in a University based Emergency department. Adult Patient fulfilled criteria of clinical gouty arthritis were included. Each patient received either oral Indomethacin or prednisolone plus placebo for 5 days. Analgesic efficacy and adverse effects in first 120min(ED phase), 1-5 days and 6-14 days were measured. The analgesic efficacy outcome was measure using visual analogue scale. Joint stiffness, joint swelling, joint tenderness, length of hospital stay, paracetamol use, and relapse rate were also measured.

Adverse events were assessed for number, duration and severity.

Results: Of 599 evaluated patients (183 excluded), 416 were included (208 patients in each arm). There was no statistical difference in pain score reduction during the ED phase (first 120 min), day 1 to 5 and day 6 to 14 between the two arms. There was no statistically significant difference in joint tenderness and stiffness score between the two arms. 34 (18%) patients in the indomethacin arm and 10 (5.3%) patients in the prednisolone group suffered from mild side effects during the ED phase(P<0.0001). 75 (39%) patients in indomethacin arm and 75 (40%) patients in the prednisolone group suffered from mild side effect during 1 to 14 days (P=0.527).

Conclusions: Prednisolone and Indomethacin both are equally effective treatments for acute gout-like arthritis in ED and show no difference in side effect rates between days 1 and 14.

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P60-Ab0002
Embryotoxicity Studies of Rhizoma Atractylodis Macrocephalae Extracts for Skeletal Malformation in Mice

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Introduction: Maternal exposure to Rhizoma Atractylodis Macrocephalae (Largehead Atractylodes Rhizome, LAR) during pregnancy induces congenital skeletal malformations in animals. We aimed to characterise the developmental toxicity of LAR, active extracts and sub-fractions and its pharmacotoxicity profiles for the skeletal anomalies were identified and evaluated.

Methods: Developmental toxicity of LAR will be characterised by bioassay-guided sub-fractionations methods. LAR extracts and sub-fractions were prepared by solvent partitions/precipitations and analysed by thin-layer chromatography. Active extracts and sub-fractions were screened by limb-bud micromass and whole-embryo culture bioassays *in vitro*; then validated by pregnant mouse model *in vivo*; and finally analysed by mass spectrometry. Chondrocyte cytotoxicity (Cyto) and differentiation (Diff); developmental morphology (Mor) and malformation (Mal); pharmacotoxicity and reproductive toxicity; underlying molecular mechanism; and chemical structures of active LAR components were determined.

Results: LAR aqueous partition (LAR-A), monosaccharide fractions (LAR-A-II) and glycosides subfractions (LAR-A-IIa and LAR-A-IIb) were more toxic than other partitions, fractions and subfractions. Average IC50Cyto and IC50Diff LAR equivalent doses were 7.68´10-16mg/ml (LAR-A), 14.20mg/ml (LAR-A-II), 24.86mg/ml (LAR-A-IIa) and 3.10mg/ml (LAR-A-IIb). Average IC50Mor and IC50Mal LAR equivalent doses were 2.66´10-15mg/ml (LAR-A), 5.50mg/ml (LAR-A-II), 7.64mg/ml (LAR-A-IIa) and 0.21mg/ml (LAR-A-IIb). Still birth and congenital skeletal malformation were induced by LAR-A-IIb. LAR suppressed expression of limb developmental genes and enhanced apoptosis in developing limb buds. Ketocycasin and glycoside derivatives were detected in both LAR-A-IIa and IIb subfractions.

Conclusions: Ketocycasin and glycosides from LAR subfractions may attribute to the developmental toxicity and induce congenital skeletal malformation in mice. Ketocycasin and its glycosides in LAR are embryotoxic and should be removed before administration.

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P61-Ab0138
Antigenic Characterisation and Epitope Mapping of the 2009 Pandemic H1N1 Influenza Virus

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A swine origin H1N1 influenza virus crossed species to infect humans and caused the first pandemic of the 21st century, as declared by the World Health Organization in June 2009. The pandemic H1N1 2009 virus is a reassortant virus containing gene segments from several sources obtained through multiple reassortment events, as yet undefined. It is likely that further viral adaptation, together with herd immunity built up through natural infections and vaccination, will drive the evolution of this novel virus in humans. Structural studies show that the hemagglutinin (HA) surface protein of the pandemic H1N1 virus is still antigenically close to that of the 1918 pandemic H1N1 virus, despite circulating in swine species for nearly 100 years. It is extremely important to monitor antigenic variations to understand how the pandemic H1N1 2009 virus evolves and interacts with its new human host. Our clinical isolates collected since 2009 revealed that the pH1N1 are antigenically homogeneous and stable according to the hemagglutination inhibition assay (HI) results. We found that amino acid substitutions at 125, 126, 128 and 185 have effect on antigenic changes among pH1N1 clinical isolates analyzed. Clinical isolates carrying D222G showed high sensitivity in binding assay with neuraminidase-treated TRBC (Turkey red blood cells), suggesting that the D222G mutation preferentially binds to SAα2,3-Gal which is mainly expressed

in the lower respiratory tract of human and more likely to cause severe or even fatal outcomes in patients. It is not known if the pH1N1 virus will maintain similar antigenic pattern along the course of evolution. Continuous surveillance for antigenic variations among clinical isolates as well as variations in the HA molecule for receptor binding properties are necessary.

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