Molecular Epidemiologic Analysis of Group A Rotaviruses in Children with Diarrhea in Wuhan City, China, 2007

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Background: Rotaviruses are the major etiological cause of acute viral gastroenteritis in infants and young children worldwide, primarily in developing countries, producing a significant disease burden.

Methods: To describe epidemiologic features and genetic characteristics of group A rotaviruses causing diarrhea in children and to estimate the relatedness or origin of the rotaviruses, a survey was conducted in Wuhan, China, 2007. A total of 889 stool specimens from diarrheal patients under 14 years old from Wuhan Children's Hospital were analyzed. Many symptoms such as vomit, cough, fever, dehydration were marked. The positive rotavirus specimens was determined by PAGE and rapid immunochromatographic assay.

Results: A total of 236 positive specimens performed further genetic analysis. Genotyping of rotavirus was determined by RT-PCR. By sequencing and phylogenetically assigning, two G9 strains were found out. In total, rotavirus detection rate of all stool specimens is 26.55% (236/889). By PAGE and rapid immunochromatographic assay, the detection coincidence rate was 86.42%. Unfortunately, the detection rate was independent of the symptoms. There were extremly significant differences of the detection rates in different age groups ($\chi^2 = 33.53$, $P < 0.01$). The detection rates in the winter season (42-64%), from October to December, were significantly higher than the other seasons($P < 0.05$). Throughout the study period, P[8] was the most frequent P serotype (88.9%), and G3 was the most frequent G serotype (75.3%), and was mostly associated with VP4 genotype P[8](68.4%). And the G-type/P-type combination G3P[8] was the most common, followed by G1P[8], G2P[4] and G3P[6]. G1 + G3P[8], G3 + G9P[8], G2 + G3P[4] and other mixed G/P types were detected also. VP7 gene sequences of G9 rotaviruses were detected out by sequencing for two strains, showed extremely high sequence identities (99—100%) to each other and to a few G9 rotavirus strains reported in Asia.

Conclusion: In our present study, the rotavirus-positive rate in children specimens was 26.55% in total. The monthly prevalence of rotavirus infection showed significant winter seasonality. It was evident that the G3P[8] rotaviruses were the most prevalent throughout the study period. These findings suggest that transmission of the G3 rotaviruses might have occurred endemically in Wuhan. The two G9 strains were phylogenetically assigned to lineage 3.

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Establishment of BALB/c Mice Model for the Acute and Chronic Forms of Human Melioidosis Caused by *Burkholderia pseudomallei*

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Burkholderia pseudomallei are the causative agent of melioidosis, a disease being increasingly recognized as an important cause of morbidity and mortality (70%) in many regions of the world. The disease is found predominantly in Southeast Asia and Northern Australia. It is highly endemic in Thailand, especially the North-Eastern part, Malaysia and Singapore. Although the first case of melioidosis in Singapore was reported in 1920 and fatal septicaemic cases of healthy young adults were reported in 1989. Acute infection is the most severe, with rapid onset of non-distinct symptoms of medical examination. We evaluated the suitability of BALB/c mice as animal models for the acute and chronic forms of human melioidosis. Five groups of eight weeks old BALB/c mice were inoculated with 150 μl of $1.2 \times 102 - 3.5 \times 108$ by intravenous; control received 150 μl of PBS. The mortality of animals was observed 12, 24, 36, 48, 96 hours. Results revealed that the lethal does 50 values of 5 cells and 2.7×105 for BALB/c mice. All the mice died within 96 h after the subsequent injection with *B. pseudomallei*. The post mortem revealed the presence of significant relatively larger more confluent, abscessation of the spleen and less frequently of the liver. Following intravenous challenge with B. pseudomallei, large abscesses with focal area of necrosis, surrounded by a rim of meshed fibrous tissues are evident by histopathologically. This study shows the BALB/c mouse strain to be highly susceptible to infection with *B. pseudomallei*. The mice suffered a rapidly-progressive bacteraemia which resulted in host death by 96 h.

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21.016

Toxoplasma gondii Infection Induces Lipid Metabolism Alterations in the Murine Host

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Background: Host lipids have recently been implicated in the pathogenesis of *Toxoplasma gondii* infection. It has been shown that cholesterol uptake from the host plasma membrane is essential for parasite replication *in vitro*. To determine if *T. gondii* infection influences the host lipid status *in vivo*, we assessed serum lipid levels at different time points during experimental *T. gondii* infection.

Methods: Groups of 6-week old female Swiss-Webster mice were infected ($n = 54$) by gavage with 8 cysts of the *T. gondii* BGD-1 strain (human origin type-2 strain) or left uninfected ($n = 18$) to serve as control. All mice were bled at day

0 and 42 post-infection (p.i.), and subgroups of 6-18 mice were bled at d7, 14, 21, and 28 p.i. for the measurement of total, HDL, and LDL cholesterol (Chl), and triglyceride levels. At d42 p.i. all surviving mice were sacrificed and brains harvested for cyst enumeration. The experiment was performed twice, and the shown data represent their cumulative results.

Results: A significant decrease ($p < 0.05$) in total Chl and HDL occurred in infected vs. control mice of d14, 21 and 42 p.i. Conversely, LDL levels were unaltered until d42, when LDL significantly increased ($p < 0.05$). While the number of cysts at the end of the experiment varied greatly (range 20—7460 per brain), a positive correlation ($p = 0.023$) was obtained between cyst counts >300 (in 44% mice) and LDL level.

Conclusion: Acute *T. gondii* infection apparently induces a decrease in reverse Chl transport. While this decrease persists up to chronicity it is only then that an increase in direct Chl transport occurs. To clarify the mechanisms underlying *T. gondii*-induced lipid metabolism alterations, our current research focuses on the analysis of Chl receptors (SR-BI and LDL-R), Apo A-IV, Apo B-100, and adiponectin, as well as the corresponding candidate genes.

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21.017

Response to a DTaP-IPV-Hib combined vaccine (Pentaxim) Given as a Booster in Thai Children Primed with an Acellular Pertussis Combination Vaccine

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Background: We assessed the immune response to Pentaxim when given as a booster dose in Thai children primed with a diphtheria, tetanus, acellular pertussis, inactivated poliovirus, hepatitis B, Hib-conjugate combination vaccine in infancy.

Methods: DTaP-IPV-Hib vaccine (Pentaxim™, Sanofi Pasteur AcXim family vaccine) was given as a 4th (booster) dose at 18—24 months of age to 156 children previously primed at 2, 4 and 6 months of age with a hexavalent vaccine containing the same vaccine antigens plus hepatitis B. A dose of monovalent hepatitis B vaccine was also given at birth. Antibody titers were measured just before and one month after the booster vaccination. Reactogenicity and safety were evaluated from parent reports.

Results: Seroprotection rates, approximately one year post-primary vaccination remained high. Anti-PRP GMT increased from 1.6 to 58.0 μg/mL pre- to post-booster vaccination. GMTs for PT and FHA increased from 3.8 to 181.2 EU/mL and from 18.0 to 289.7 EU/mL respectively. GMTs for each poliovirus type also strongly increased from pre- to post-booster dose. Vaccine reactogenicity was low. There were only two severe local reactions and two subjects had severe fever possibly related to vaccination, all of which resolved.

Conclusion: Pentaxim induced a strong booster response to all the vaccine antigens at 18-24 months and was well tolerated. The timing of this booster was appropriate as pre-booster antibody titres and seroprotection rates remained satisfactory. Booster vaccination during from the second year of life has been recommended and is the practice in many different countries, with the aim of expanding control of childhood infectious diseases including pertussis and Hib. [study E2I36]

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21.018

An Acellular Pertussis, Diphtheria, Tetanus, Inactivated Poliovirus, Hib-Conjugate Combined Vaccine (Pentaxim) at 2, 4, and 6 Months of Age Plus Hepatitis B at Birth, 2, and 6 Months of Age in Infants in Thailand

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Background: We evaluated the immunogenicity and safety of a pentavalent acellular pertussis, inactivated poliovirus-based combination vaccine in a tropical country, with concomitant administration of hepatitis B vaccine.

Methods: The pentavalent combination vaccine Pentaxim™ (sanofi pasteur, AcXim family vaccine), containing diphtheria, tetanus, acellular pertussis, inactivated poliovirus, and *Haemophilus influenzae* type B conjugate (PRP-T) antigens was given to 186 Thai infants at 2, 4 and 6 months of age. Hepatitis B vaccine was given at birth, 2 and 6 months of age, following the national schedule. Immunogenicity data from French infants vaccinated with the same schedule was used as a reference. Antibody titers were measured one month after completing the three-dose primary vaccination. Reactogenicity and safety were evaluated from parent reports.

*Results:*After the third dose, anti-PRP ≥ 1.0 μg/mL was observed in 96.5% (95%CI 92.6; 98.7) of subjects (GMT = 9.3 μg/mL). Anti-polio GMTs were 120, 1553 and 3003 1/dil U. for poliovirus types 1, 2 and 3 respectively. Two-fold increase from pre- to post-vaccination in antibody concentration were 97.6% and 97.7% for PT and FHA respectively. Anti-PT and anti-FHA GMTs increased from 2.8 to 176 EU/mL, and from 3.7 to 119 EU/mL respectively. Anti-pertussis PT and FHA antibody titers ≥ 25 EU/mL were observed in 100% and 98.8% of subjects, respectively. Hepatitis B seroprotection rate (anti-HBs ≥ 10 mIU/mL) was 100% (95%CI 97.5%; 100%) with a GMT of 1561 mIU/mL (95%CI 136; 1783 mIU/mL). Vaccine reactogenicity was low, with fewer than 1% of vaccine doses eliciting a severe solicited adverse reaction. No case of hypotonic hyporesponsive episode was reported. There were no drop outs because of adverse events.

Conclusion: The immunogenicity of Pentaxim, when given at 2, 4 and 6 months of age in the tropical climate of Thailand was high, and similar to responses in European infants. The vaccine was well tolerated even when given concomitantly at separate sites with hepatitis B vaccine [NCT00254969].

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