Results: The recruitment started in June 2006. By January 2008, 201 longitudinal serum specimens collected from mothers, neonates, and 6-month-old babies (one mother delivered twins) have been measured with EV71 neutralizing antibody titters. The seropositive rates (percentage of antibody titer $\geq 1:8$) in mothers, neonates, and 6-month-old babies were 61% (122/201), 46% (93/202), and 30% (60/200), respectively. Geometric mean titers (95% confidence intervals) of serum EV71 antibody in mothers and neonates were 10.2 (8.7, 11.5) and 8.5 (7.4, 9.7), respectively.

Conclusions: In northern Taiwan, only 46% of neonates have protective antibody against EV71 and these maternal antibody titers have declined to undetectable level (<8) by 6 months of age. Historical data in the 1998 epidemic also showed that infants under 1 year old had the highest risk of severe EV71 infection. Therefore, development of EV71 vaccines in Taiwan should target infants under 6 months old.

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46.023

Community-Acquired Poliovirus Infection in Immunocompromized Children Following National Immunization Days in Tunisia

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The global polio eradication program recommends the use of massive vaccination campaigns with live vaccine through National Immunization Days (NIDs) to displace the wild virus from the community. Immunodeficient patients may be indirectly infected and become chronic excretors and potential reservoirs of polioviruses, a concern for the post eradication era. This prospective study aimed to assess the risk of community-acquired infection of immunodeficient patients following NIDs, the dynamics of viral excretion and the genetic variation of excreted viruses. Sixteen children with various primary immunodeficiencies, who did not receive the vaccine during the campaign, were investigated. Stool samples were collected weekly, shortly after the NIDs, during at least three months and processed for viral isolation. Isolates were characterized by three intratypic differentiation methods and partial sequencing of the VP1/2A region. Polioviruses were detected in 4 out of 16 patients (serotype1 in 3 patients and serotype3 in one patient). Sequencing revealed more than 99% homology with homotypic Sabin strains suggesting recent infection. Duration of viral excretion ranged from 1 to 7 weeks. Nine out of eleven isolates from the 3 polio1-infected patients disclosed a Non Sabin Like phenotype by ELISA and had recurrent mutations within or close to the neutralizing antigenic sites. The risk of secondary infection in immunodeficient patients is within the range reported for the general population. Although none of the four infected patients developed prolonged viral excretion, particular viral variants were selected and may be of epidemiological significance.

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46.024

Broad-Spectrum Antiviral Activity of Nucleic Acid-Based Antiviral Agents Against Avian and Seasonal Influenza Viruses

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The increasing prevalence of influenza viruses resistant to antiviral drugs such as amantadine and oseltamivir undermines our ability to defend against future influenza pandemics. There is an urgent need to develop novel antiviral agents which are robust and offer broad-spectrum protection against the ever changing influenza viruses. The objective of this study is to evaluate the in vivo antiviral efficacy of nucleic acid-based immunomodulators such as Polyclonal Synthetic Double-Stranded RNA (ICLC) and oligonucleotides containing unmethylated CpG using a mouse lethal infection model with influenza A/PR/8/34 (H1N1) and/or with the highly pathogenic avian influenza H5N1 (H5AI) viruses. Groups of BALB/c mice were pre-treated intranasally with 1 or 2 doses of liposome-encapsulated Poly ICLC (LE-Poly ICLC, 20 μg/dose/mouse) or with CpG (5 μg/dose/mouse) oligonucleotides. At various times post pre-treatment, the animals were challenged intranasally with multiple doses of influenza A/PR/8/34 or with HPAI viruses, and survival rates of control and pre-treated mice were compared at day 14 post infection. Pre-treatment with liposome-encapsulated Polyclonal ICLC provided complete protection against 10 LD50 influenzaA/PR/8/34 and 1 LD50 dose of HPIA virus. When the challenge dose of HPIA was increased to 4 LD50, the protection provided by LE-Poly ICLC was 63–75% ($p < 0.001$ vs control), with all control mice succumbing to the infection. Pre-treatment with CpG oligonucleotides provided complete protection to mice against 5 LD50 influenza A/PR/8/34. The window of protection (the time interval between drug pre-treatment and virus challenge) was 21 days for LE-Poly ICLC and 4 days for CpG oligonucleotides, respectively. RT-PCR analyses of mouse lung tissues from LE-Poly ICLC treated mice showed activation of toll-like receptor-3 pathway, and induction of cytokines including IL1-α, -β, IFN-γ, TNF-α, among others. Collectively, these results suggest that LE-Poly ICLC can provide broad-spectrum protection and may have an important role in protecting against avian or seasonal influenza infections.

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