short- and long-term adverse effects of anti-HIV medications, and the difficulty of maintaining adherence to complex regimens containing unpalatable formulations of limited potency. As these obstructions are overcome, it is prudent to reconsider early initiation of ART with lifelong maintenance. Of interest, this reviewer’s experience finds that children started on ART at younger than 1 year of age and adherent to their regimen are among the only patients who normalize their CD4:CD8 ratio. The relevance of this finding is yet to be clarified but suggests more effective immune reconstitution in children treated early in their course.

Prevalence of Congenital Anomalies in Infants With In Utero Exposure to Antiretrovirals

PURPOSE OF THE STUDY. The use of effective, fully suppressive antiretroviral (ARV) therapy during pregnancy dramatically lowers mother-to-child transmission of HIV. Currently, nucleoside reverse transcriptase inhibitors form the foundation of ARV combination therapy for pregnant women; however, these drugs have potential negative consequences for the developing fetus. This study examined the prevalence of congenital anomalies in infants who were exposed in utero to ARV drugs.

STUDY POPULATION. International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT) protocol P1025 is a prospective, observational study of infants born to HIV-infected mothers. The current study population included 1112 singleton infants enrolled in P1025 for whom the congenital anomalies case-report form had been completed.

METHODS. Affected infants were identified through computerized screening of the case-report form. These cases were then reviewed and classified by a panel of clinicians who were not aware of the mother’s ARV exposure during pregnancy.

RESULTS. Eighty congenital anomalies were identified in 1112 infants, resulting in a congenital anomaly rate of 5.49 per 100 births and included: cardiovascular (33), musculoskeletal (15), renal (9), genitourinary (6), craniofacial (4), and central nervous system (2) events. The only specific ARV drug association was with efavirenz, a known teratogen.

CONCLUSIONS. ARV use during pregnancy has been associated with increased risks for prematurity and mitochondrial toxicity. A number of studies (reviewed in the current report) have documented that the congenital anomaly prevalence rate in infants born to HIV-infected mothers is significantly higher than for the general US population (~3 per 100 live births). Cardiovascular anomalies were most frequent, and except for efavirenz, no significant association between in utero exposure and congenital anomalies was identified.

Performance of HIV-1 DNA or HIV-1 RNA Tests for Early Diagnosis of Perinatal HIV-1 Infection During Anti-retroviral Prophylaxis

PURPOSE OF THE STUDY. The identification of HIV-derived nucleic acid in the blood of perinatally exposed infants is the most sensitive and specific method for the early detection of HIV infection in this population. HIV DNA is measured in peripheral blood mononuclear cells and HIV RNA in the plasma. This study compares the performance of HIV DNA polymerase chain reaction (PCR) and HIV RNA PCR for the diagnosis of HIV infection in exposed infants.

STUDY POPULATION. A total of 1567 children, representing a subgroup born to HIV-infected women, were enrolled in a prospective, multicenter, French perinatal cohort.

METHODS. Plasma HIV RNA and peripheral blood mononuclear cell HIV DNA were measured by using standard assays generally obtained at birth and then at 1, 3, and 6 months of age in the absence of breastfeeding.

RESULTS. A total of 1502 infants were considered uninfected at 6 months of age, and 65 were considered infected. The following table demonstrates the ability of the 2 assays to identify infection in these 65 patients.

<table>
<thead>
<tr>
<th>Age</th>
<th>Positive DNA PCR, %</th>
<th>Positive RNA PCR, %</th>
<th>Either Positive, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 d</td>
<td>55</td>
<td>58</td>
<td>62</td>
</tr>
<tr>
<td>1 mo</td>
<td>89</td>
<td>89</td>
<td>91</td>
</tr>
<tr>
<td>3 mo</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>6 mo</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>
Neither maternal antiretroviral therapy nor postnatal prophylaxis affected PCR results at <7 days and at 3 months of age. It is important to note that these mothers were undergoing regimens that were not fully suppressive, and 50 of the 65 patients were not receiving highly active antiretroviral therapy consisting of at least 3 drugs. DNA PCR and RNA PCR resulted in equal sensitivity. DNA PCR was associated with 2 false-positive results at 3 and 4 days of age. The positive predictive value at <7 days of age was 100% for HIV RNA PCR and 78% for DNA PCR; at 1 month of age, both tests had positive predictive values of 100%. Negative predictive values for both tests were 99.5% at <7 days, 99.8% at 1 month, and 100% at 3 months of age.

CONCLUSIONS. Both HIV DNA PCR and HIV RNA PCR resulted in similar sensitivities and specificities at 1 and 3 months of age. Importantly, 11% of infected children had negative PCR results at age 1 month regardless of assay used.

REVIEWER COMMENTS. Both assays seem to be equally effective in identifying HIV infection in infants exposed perinatally to HIV. In general, reference laboratories are more familiar with RNA PCR. This situation would be the primary justification for use of RNA PCR in the community.

Cost-Effectiveness of Oseltamivir Treatment for Children With Uncomplicated Seasonal Influenza


PURPOSE OF THE STUDY. To evaluate the cost-effectiveness of oseltamivir treatment for seasonal influenza in children and consider the impact of oseltamivir resistance on these findings.

STUDY POPULATION. Unvaccinated children, stratified according to age groups (12–23 months, 2 years, 3–4 years, 5–11 years, and 12–17 years) visiting a physician’s office with age-appropriate symptoms of uncomplicated influenza-like illness.

METHODS. The investigators developed a model to evaluate 1-year clinical and economic outcomes associated with 3 outpatient management strategies for unvaccinated children with influenza-like illness: no antiviral treatment; diagnostic testing and oseltamivir treatment when results were positive; and empiric oseltamivir treatment. The model depicted a hypothetical nonpandemic influenza season with a 29% level of oseltamivir resistance in circulating viruses and 14% to 54% probability of seasonal influenza with influenza-like illness. Strategies were compared by using incremental cost-effectiveness ratios.

RESULTS. In the preliminary analysis, empiric oseltamivir treatment consistently produced the greatest benefit. The incremental cost-effectiveness of this alternative, compared with testing and treating, was <$100,000 per quality-adjusted life-year gained in all age groups except the oldest. The testing strategy was consistently more effective compared with no treatment, and it costs between $25 900 and $71 200 per quality-adjusted life-year gained, depending on age. Results were sensitive to the prevalence of oseltamivir resistance in circulating viruses.

CONCLUSIONS. Empiric oseltamivir treatment of seasonal influenza is associated with favorable cost-effectiveness ratios, particularly in children aged 1 to <12 years. However, ratios are highly dependent on the prevalence of oseltamivir resistance among circulating influenza viruses.

REVIEWER COMMENTS. What a breath of fresh air to find this very interesting and clinically relevant article that examined a cost-effective analysis which deals with how to best manage children presenting for medical attention with influenza-like illness. Despite the availability of rapid diagnostic testing, which is not always the most sensitive or specific, relying on clinical diagnosis and being aware of the level of oseltamivir resistance of circulating influenza viruses seems to be the ideal approach here. What a novel concept: relying on one’s clinical diagnostic skills to deal with these types of patients.

Treatment of Neonatal Sepsis With Intravenous Immune Globulin


PURPOSE OF THE STUDY. Neonatal sepsis is a major cause of death and complications despite antibiotic treatment. Effective adjunctive treatments are needed. Newborn infants are relatively deficient in endogenous immunoglobulin. Meta-analyses of trials of intravenous immunoglobulin for suspected or proven neonatal sepsis suggest a reduced rate of death from any cause, but the trials have been small and of varied quality.

STUDY POPULATION. At 113 hospitals in 9 countries, 3493 infants receiving antibiotics for suspected or proven serious infection were enrolled.

METHODS. Participants were randomly assigned to receive 2 infusions of either polyvalent immunoglobulin G (at
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The online version of this article, along with updated information and services, is located on the World Wide Web at:
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